In previous papers we have discussed the ferment changes that occur in dogs during trypsin, anaphylactic, and kaolin shock, noting more particularly the relation of the serum protease to the antiferment and to the split products contained in the serum, together with changes in the lipase content. In the present paper we shall present the resulting ferment changes following the injection of various protein derivatives.

The fundamental ideas of Vaughan relating to the toxicity of protein split products have been fully developed during the course of the last few years; the only element of uncertainty lies in the interpretation of certain phases of specificity of ferments which are supposed to split the native protein to toxic fragments. According to Vaughan's hypothesis, specific protease is produced capable of such function, a supposition which has received much support from the work of the Abderhalden school. There is, however, certain experimental evidence to the contrary, indicating that the specific element is not due to specific ferment action, but rather that the splitting that occurs is due to a non-specific ferment; that the split products are largely derived from the serum proteins and not from the injected antigen; while the element of specificity lies in the colloidal changes which bring about a lowering of the antiferment titer and in the rapid mobilization of the protease.

1 Vaughan, V. C., Vaughan, V. C., Jr., and Vaughan, J. W., Protein Split Products in Relation to Immunity and Disease, Philadelphia and New York, 1913.
Effect of Protein Split Products.

Text-Fig. 1. Text-Fig. 1 a. Text-Fig. 1 b.

Text-Figs. 1, 1 a, and 1 b. Serum changes following intravenous injections of (Text-fig. 1) proto-albumoses, (Text-fig. 1 a) primary proteoses, (Text-fig. 1 b) secondary proteoses.
While it is true that every protein when hydrolyzed will yield toxic substances, there is considerable variation in the degree of toxicity of the derivatives from different proteins. According to Baehr this difference has some relation to the chemical configuration of certain components of the fragments. It has been found that of the various split products the primary proteoses are in general most toxic (Zunz, Jobling and Strouse, Zunz and György), the secondary proteoses being much less toxic. While shock produced by the split products is usually called peptone shock, the peptones, as a rule, are less toxic than the primary proteoses. The peptone preparation which we have used was, however, an exception to this statement, displaying an instantaneous and marked toxicity. It was prepared from dog muscle by the usual method.

The technique used in these experiments has been fully described previously, so that a repetition will be superfluous.

**EXPERIMENTAL.**

**Effect of Primary Proteoses.**

Dog 28.—Weight 7 kilos. 0.2 gm. of proto-albumoses (prepared by peptic digestion of dog serum) was injected intravenously at 9.45 a.m. The dog showed practically no evidence of malaise, although there was a slight primary fall in the leucocytes with a rise during the afternoon.

There was practically no change in the ferments and the antiferments; the non-coagulable nitrogen decreased slightly, although the amino nitrogen and the proteoses were unaltered.

Dog 70.—Weight 8.1 kilos. 0.5 gm. of proto-albumoses (from Witte's peptone) was injected intravenously at 8.20 a.m. The dog became nauseated and vomited almost immediately; it showed extreme prostration during the afternoon and died during the night (Text-fig. 1).

Dog 71.—Weight 6.6 kilos. 0.5 gm. of primary proteoses (from Witte's peptone) was injected intravenously at 9 a.m. Manifestations of intoxication were the same as in Dog 70. Death occurred during the night (Text-fig. 1 a).

In both these experiments there will be noted an immediate rise in the antiferments with a subsequent fall; a mobilization of protease more marked in Dog 71; a rather sharp rise in the serum lipase; and a distinct decrease in the serum proteoses and amino nitrogen. It is

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Effect of Protein Split Products.

It is rather curious that the injection of 0.5 of a gram of proteoses should be followed by the decrease in the amount of the proteoses in the serum.

Effect of Secondary Proteoses.

Dog 73.—Weight 6 kilos. 0.5 gm. of secondary proteoses (from Witte's peptone) was injected at 10:50 a. m. The dog became somewhat nauseated but did not show the extreme prostration that characterized the two previous dogs; it showed no ill effects the following morning.

It will be observed (Text-fig. 1 b) that there occurred a well marked rise in serum protease, while the lipase was not affected. Proteoses were increased during the afternoon, but returned to normal the following morning. The amino nitrogen showed only a slight primary decrease.

Effect of Peptone.

Dog 74.—Weight 15 kilos. 0.25 gm. of muscle peptone injected at 9 a. m. (Text-fig. 2). The animal was immediately prostrated and was nauseated, after which it rapidly recovered and showed no further ill effects.

As will be observed from Text-fig. 2 there was almost an immediate rise in protease with a following decline. The antiferment showed rather a marked fluctuation, while the lipase showed only a slight rise with a fall in titer later. The proteoses were at first decreased but increased during the afternoon. The amino nitrogen showed only a slight increase.

Dog 43.—Weight 7 kilos. 0.17 gm. of muscle peptone was injected intravenously at 11:30 a. m. (Text-fig. 2 a). The animal became ill in a manner similar to Dog 74, and later developed a paresis of the hind legs. Died at 5 p. m.

In this animal the intoxication was more evident, both in its effect on the temperature and leucocyte curve, and in its effect on the serum ferments.

Dog 47.—Weight 4.5 kilos. This animal was given a very small dose (0.05 gm.) of muscle peptone intravenously at 9 a. m., without ill effects of any marked degree except an initial nausea and prostration (Text-fig. 2 b).

In contrast to the two previous dogs, however, there was a constant fall in the antiferment titer with a recovery the following day,
Text-Fig. 2. Serum changes following the intravenous injection of dog muscle peptone.
while the protease showed at first a decline and an increase during the afternoon. The lipase was not increased.

When introduced into the stomach or rectum (0.5 of a gram) the peptone was without toxic effect, and produced no alteration in the serum. When injected directly into the lumen of the small intestines, however, death resulted within five to ten minutes, the animal presenting the picture of profound shock.

CONCLUSIONS.

1. In dogs the toxic effect of primary proteoses is usually associated with the following serum changes: (a) an increase in serum antiferment, with a following fall in titer; (b) some increase in serum protease; (c) an increase in serum lipase; (d) a decrease in serum proteoses and amino nitrogen.

2. Secondary proteoses produce (a) less marked changes in the antiferment titer; (b) a marked increase in serum protease; (c) an increase in serum proteoses; (d) only a slight change in serum lipase; (e) a primary decrease in amino nitrogen.

3. The peptone which we have used (prepared from dog muscle) caused (a) a change in antiferment titer similar to that produced by the primary proteoses; (b) a marked increase in serum protease; (c) only a slight increase in serum lipase; (d) a primary decrease in proteoses, followed by an increase later; (e) an increase in amino-acids.

4. A very small dose of peptone resulted in a decrease in antiferment titer, together with a primary decrease in serum protease.

5. The peptone preparation was non-toxic when introduced into the stomach or rectum, while the intestinal injection was followed by an immediate intoxication.

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