

These studies indicate that in old rats of this strain there is a tendency for atypical areas of hypertrophied cells to appear. The cells in these areas are histologically similar to those found in the adenomata of the pituitary described above.

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### Observations on Dolman's Test for Determining the Presence of Staphylococcal Enterotoxin.

R. H. RIGDON. (Introduced by Roy C. Avery.)

*From the Department of Pathology, Vanderbilt University Medical School, Nashville, Tenn.*

Numerous observations indicate that staphylococci are frequently present in cases of food poisoning. It is often difficult, however, to determine whether or not this organism is the etiological agent. The studies of Jordan and McBroom,<sup>1</sup> Woolpert and Dack,<sup>2</sup> and Dolman, Wilson and Cockcroft,<sup>3</sup> suggest that toxin produced by staphylococci is responsible for the clinical symptoms. Little is known about the pathological lesions in cases of food poisoning resulting from staphylococci because only one death has been reported.<sup>4</sup>

Dolman and his associates<sup>3</sup> published a method by which they could determine whether or not the staphylococcus found in the food in cases of poisoning is the etiological agent. Furthermore, with this test they showed that the gastro-intestinal fraction in staphylococcal toxin was not destroyed by heat for 20 minutes at 100°C. The thermolability of this fraction is very different from that of the hemolysin, leucocidin and skin-necrotizing fractions. The technic of this test consists in injecting intraabdominally into kittens toxin prepared from the cultures of staphylococci. If the animal shows marked lassitude and weakness, with unsteadiness which appears shortly after the injection and if these symptoms culminate in the first of a series of intermittent paroxysms of

<sup>1</sup> Jordan, E. O., and McBroom, J., *PROC. SOC. EXP. BIOL. AND MED.*, 1931, **29**, 161.

<sup>2</sup> Woolpert, O. C., and Dack, G. M., *J. Inf. Dis.*, 1933, **52**, 6.

<sup>3</sup> Dolman, C. E., Wilson, R. J., and Cockcroft, W. H., *Canad. Public Health J.*, 1936, October, 489.

<sup>4</sup> Blackman, S. S., *Bull. Johns Hopkins Hosp.*, 1935, **57**, 289.

vomiting, associated with diarrhea, then the toxin contains a gastro-intestinal poison.

Stone<sup>5</sup> has recently suggested a bacteriological method for distinguishing staphylococci that produce a gastro-intestinal toxin. The results of Dolman and his associates differ from those of Stone.

I have been unable so far to separate satisfactorily the different components which have been described as occurring in staphylococcal toxin. Dolman's test seemed to offer a satisfactory method to differentiate the gastro-intestinal from the other fractions in one of the toxin-preparations I have been studying.

The toxin\* was prepared by a method very similar to that used by Dolman. The control was the uninoculated medium.\* This medium was centrifuged and the supernatant fluid was used for the inoculations. Puppies weighing from 1500 to 2500 gm. and kittens from 750 to 1150 gm. were injected intraabdominally. The toxin was heated at 100°C. for 2 hours.

Two puppies were given 5 cc. of the heated toxin and 2 were given 10 cc. Three puppies were given 10 cc. of the control medium. The majority of these animals were drowsy for approximately 4 hours thereafter. None inoculated with heated toxin vomited. Each of the 3 given the control medium vomited one or more times during the first 30 minutes of the experiment. All the 7 puppies appeared normal after 18 to 24 hours except one which had a diarrhea.

These puppies were again injected after 24 hours with the following preparations: Five were given 5 cc. of the control medium and 2 were given an equal quantity of staphylococcal toxin. All were sick immediately after the inoculation. Four of the 5 receiving the control medium vomited several times during the first 30 minutes. The fifth puppy never vomited. Both dogs given the toxin vomited within a period of one hour and one developed severe abdominal cramps and a diarrhea. After 4 hours the group given the control medium appeared normal except for one which had loose stools. Both of the puppies inoculated with the toxin were dead after 4 hours. The pathological changes in these were similar to those previously described following the intravenous injection of staphylococcal toxin.<sup>6</sup>

Four kittens were given intraabdominally 5 cc. of the control medium and 2 vomited within a period of 30 minutes. Three were inoculated with 5 cc. of staphylococcal toxin and each vomited with-

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<sup>5</sup> Stone, R. V., *PROC. SOC. EXP. BIOL. AND MED.*, 1935, **33**, 185.

\* Supplied by Lederle Laboratories.

<sup>6</sup> Rigdon, R. H., *Arch. Path.*, 1935, **20**, 201.

in 5 minutes. Three kittens were given a similar quantity of the toxin after it had been heated for 2 hours at 100°C. and none vomited. A majority of the kittens were drowsy and weak after each of the inoculations. One that received the control medium had a diarrhea after 24 hours. The 3 kittens given the staphylococcal toxin grew progressively weaker and all were dead after 4 hours. The pathological changes were similar to those in the puppies.

The fact that the kittens and puppies were sick, vomited, and had a diarrhea following the intraabdominal injection of 5 cc. of staphylococcal toxin indicates, according to Dolman's test, the presence of an enterotoxin. Three kittens given 5 cc. of heated toxin and 2 dogs given an equal volume of the same toxin and 2 other dogs given twice this amount did not vomit. Four out of a group of 5 puppies given 5 cc. of the control medium vomited within a period of 30 minutes. Of a group of 7 kittens given the control medium, 2 vomited.

Since some of the kittens and dogs in this study were sick and vomited following injection of the control medium it would appear impossible to determine whether or not they vomited from the effect of the toxin or from the effect of the medium. Furthermore it does not seem correct to conclude that staphylococcal enterotoxin is thermostable. In this study none of 4 dogs or 3 kittens vomited after receiving the heated toxin.

The volume of the material injected and the individual variation in animals of the same species may account for the observations that have been made in an attempt to separate the staphylococci into 2 groups: those which do and those which do not produce an enterotoxin.

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### Cataphoretic Separation of Toxic Components of Moccasin Venom.

WALTER MARX AND SAMUEL M. PECK.

*From the Laboratories of the Mount Sinai Hospital, New York City.*

Attempts at separation of the various active components of snake venoms have not been very successful. These principles are probably proteins or substances closely related to proteins.<sup>1</sup> They are quite

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<sup>1</sup> Peck, S. M., and Marx, W., publication in preparation.