ing drop preparations of heavy water and into 2 controls with distilled water. Over a period of 48 hours no difference in motility could be observed between the heavy water and control ordinary water preparation.

7534 P

Depressor Substances in Peritonitis.

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There is little experimental work to substantiate the clinical belief that death from peritonitis is due to vasomotor collapse incident to absorption of toxins from the peritoneum. Zinnser, Parker and Kuttner[1] and Branham[2] both demonstrated that *Escherichia coli* produced a soluble toxic substance. Steinberg and Ecker[3] and Steinberg[4] have emphasized the rôle of bacterial toxins in peritonitis. Steinberg and his co-workers[5] have demonstrated a slight blood pressure fall in early peritonitis. Scott and Wangensteen[6] have showed that the peritoneal exudates from uncomplicated experimental intestinal obstruction were innocuous.

It occurred to us that the vasomotor system of the host might be less sensitive than that of a normal animal to the toxic substances developed in the peritoneal cavity. Peritonitis was induced in 17 dogs by the method of Buchbinder, Heilman and Foster[7] which consists of leaving an open loop of ileum with intact blood supply free in the peritoneal cavity. An end to end or a lateral anastomosis is made around the loop to restore the continuity of the intestinal

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[1] Zinnser, H., Parker, J. T., and Kuttner, A., PROC. SOC. EXP. BIOL. AND MED., 1920, **18**, 49.

[2] Branham, S. E., *J. Infect. Dis.*, 1925, **37**, 538.

[3] Steinberg, B., and Ecker, E. E., *J. Exp. Med.*, 1926, **43**, 443.

[4] Steinberg, B., *Arch. Surg.*, 1931, **23**, 145.

[5] Steinberg, B., Kobacker, J. L., and Russel, T. G., PROC. SOC. EXP. BIOL. AND MED., 1930, **30**, 1155.

[6] Scott, H. G., and Wangensteen, O. H., PROC. SOC. EXP. BIOL. AND MED., 1932, **29**, 559.

[7] Buchbinder, J. R., Heilman, F. R., and Foster, G. C., *Surg. Gyn. and Obst.*, 1931, **53**, 726.

tract. Bile peritonitis was induced in 9 dogs by 3 methods: by the intraperitoneal injection of whole sterile dogs' bile, by the similar administration of a sterile bile salt solution and by ligature of the common bile duct followed by defundation of the gall bladder. Twenty-three specimens of peritoneal washings or of peritoneal exudates were obtained by aseptic lavage of animals with suppurative peritonitis some time prior to death. These fluids were then centrifuged at high speed until clear and the supernatant fluid injected intravenously into normal dogs under barbital or urethane anesthesia. In a few instances the supernatant fluid was passed through a Mandler filter of porosity corresponding to a Berkefeld-N filter. Since the effect on blood pressure of the Mandler filtrates differed only quantitatively from the centrifuged supernatant fluid, the 2 will be considered collectively. As a control 18 fluids were obtained by aseptic lavage of the peritoneal cavity of 13 normal dogs. Extracts were made by the method of Chang and Gaddum[8] of the whole peritoneal washings, the supernatant fluids, and of the centrifuged sediment from all the above materials.

The symptoms described by the investigators[1-3] who demonstrated the presence of the soluble toxic substance of *Escherichia coli* are compatible with those produced by a profound drop in blood pressure. Accordingly, we have also investigated the hemodynamic effects of bacterial filtrates of broth cultures of *Escherichia coli* and of a hemolytic streptococcus freshly isolated from a case of streptococcus peritonitis in man. Extracts by the method of Chang and Gaddum[8] were also prepared of the corresponding bacterial sediments in several instances. Peptone-free veal infusion broth was used for the nutrient medium. Aerobic and anaerobic cultures were made in every instance when the peritoneal cavity was opened. In those cases where a significant drop in blood pressure was obtained upon injection of the peritoneal washings into a normal dog there was a heavy growth of *Escherichia coli* with or without a growth of an obligate anerobe resembling *Clostridium welchii.*

Results. *(a) Peritonitis induced by an open intestinal loop.* In 15 instances taken from tests of the 23 specimens of peritoneal washings from dogs with peritonitis produced by an open intestinal loop, there was a profound but variable immediate drop in blood pressure of from 18 to 80 mm. of mercury. Three specimens obtained post-mortem varied from the others in that the latter samples were tainted by the odor of putrefaction. These latter 3 gave an especially rapid and profound drop in blood pressure. A considera-

[8] Chang, H. C., and Gaddum, J. H., *J. Physiol.*, 1933, **79**, 255.

tion of the first appearance of vasodepressing substance indicates that an appreciable time is required to develop vasodepressing substances in the peritoneal content. The control washings from normal dogs and from those in which peritonitis was not present had no effect upon the blood pressure of another dog.

(b) Bile Peritonitis. The centrifuged exudate or the combined exudate and washings removed from 8 dogs in which bile peritonitis was present had no depressing effect on the blood pressure of other dogs, while in a single instance vasodepression was noted with a fluid obtained from an animal that had died a few hours prior to lavage of the peritoneal cavity.

(c) Extracts of Peritoneal Exudates, Washings and Sediments. Extracts of these materials prepared according to the method of Chang and Gaddum[8] demonstrated the presence and concentration of a vasodepressing substance in the whole exudate and in the centrifuged sediments at all times, both from the bile peritonitis animals and those with suppurative peritonitis. A vasodepressant extract was obtained from the supernatant centrifuged fluid only when that fluid itself contained such substances. Bacterial sediments contained no vasodepressing substance. The finding of such a substance in normal mammalian tissues is in agreement with the finding of such substances by Harkins and Harmon.[9]

(d) Bacterial Filtrates. Without exception a vasodepressing substance with a delayed time of action of 20 to 45 minutes after injection was present in Mandler filtrates of *Escherichia coli.*

7535 P

Mutual Influence of Crystalloids of Human Blood Serum on Their Equilibrium.

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The blood serum is an aqueous (ultramicroscopic)-suspension of colloids in a solution of crystalloids. The crystalloids are under normal conditions in a well balanced equilibrium, which is sustained by the colloids: static equilibrium. A normal blood serum for

[9] Harkins, H. N., and Harmon, P. H., PROC. SOC. EXP. BIOL. AND MED., 1934, **32**, 6.