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.*

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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.

instance contains 90-120 mg. of dextrose per 100 cc. of blood. The presence of the colloids inhibits even *in vitro* an increase of this amount within certain (physiological) limits. If we try to increase the blood sugar by adding the physiological amount of 100 mg. per 100 cc. and determine the sugar we find only 25% of the added amount; 75% (60-80%) disappear in the normal human serum. The serum colloids have, therefore, the power to restore and to maintain the equilibrium, if we try to disturb it: dynamic equilibrium. The following studies are based on this observation. The serum crystalloids are electrolytes and non-electrolytes. The influence of changes of the electrolytes as well as of the non-electrolytes on the static and on the dynamic equilibrium of the non-electrolytes of the normal human blood serum has been studied with the following results:

(1) Influence of cations on the static equilibrium of the serum sugar: Chlorides have been used in n/10, n/100 solution, 0.02 cc. added to 1 cc. of serum. NaCl does not influence the blood sugar even in n-solutions. KCl increases the blood sugar (5-10%), $CaCl_2$ and $MgCl_2$ do not influence the sugar as a rule, but act differently in different sera. $FeCl_3$ always decreases the sugar of a normal serum, ca. 10%.

(2) The influence of cations on the dynamic equilibrium of the serum sugar, *i. e.*, after the addition of a physiological quantity (200 mg. per 100 cc.) acts exactly in the same way, but more intensely; NaCl does not influence the loss of the added dextrose, KCl decreases the loss considerably, $CaCl_2$ and $MgCl_2$ also decrease the loss, but less than KCl; $FeCl_3$ always increases the loss of dextrose.

(3) Influence of anions on the static equilibrium of the serum sugar: The neutral sodium salts of the anions have been added in the same amounts as used in the cations (n/10 solutions, 0.02 cc. to 1 cc. of serum). Chloride and carbonate do not influence the serum sugar, phosphate and sulphate liberate sugar in a similar way as KCl; Na_2SO_4 has a stronger action than Na_3PO_4.

(4) Influence of anions on the dynamic equilibrium of the serum sugar: The only salt which had a marked influence was Na_2SO_4, which decreased the loss of dextrose considerably.

(5) Influence of cations on the static equilibrium of the urea of the serum: $FeCl_3$ has a pronounced decreasing influence upon the urea of the serum, $CaCl_2$ has no influence, $MgCl_2$ and also KCl do not influence, as a rule, the original urea of the serum, there are, however, considerable differences among the different sera.

(6) Influence of cations on the dynamic equilibrium of urea:

Urea added to the serum can be quantitatively recovered; there is no loss like in dextrose. $FeCl_3$ causes a loss of the urea added, the other cations do not influence the dynamic equilibrium.

(7) Influence of anions on the static equilibrium of urea: Na_2CO_3 causes a loss of ca. 10%, Na_2SO_4 and Na_3PO_4 cause a loss up to 50% of the original urea of the serum.

(8) Influence of the anions on the dynamic equilibrium of the urea: The 3 sodium salts examined all had the same influence on the urea, causing the loss of about 7% of the urea added.

(9) There is an interesting antagonism between the serum dextrose and the serum urea, concerning their influences on cations and anions: Adding of dextrose increases the influence of cations and nullifies the influence of anions on urea. Adding urea decreases the influence of cations on dextrose, nullifies the influence of Na_2SO_4, but intensifies the influence of Na_2CO_3 and of Na_3PO_4 on dextrose.

(10) Influence of non-electrolytes on non-electrolytes (mutual influence of dextrose and urea): Adding dextrose to the serum causes a loss of dextrose, as mentioned, as high as 75%. It does not, however, influence the serum urea (static equilibrium). There is no loss of urea, when urea is added (30 mg. per 100 cc.), and none of dextrose. The simultaneous addition of urea and dextrose does not alter the loss of dextrose which remains 75%, but causes a loss of the added urea (dynamic equilibrium) between 30 and 50% in a normal human serum.

All these experiments have been checked in aqueous solutions. The presence of the serum colloid is essential for the results. According to previous studies of the author[1] it is very likely that the struggle for water between the highly hydrophilic and even hygroscopic electrolytes and non-electrolytes plays an important rôle in the maintenance of their equilibrium in the presence of serum. The quantities added were exceedingly small: 0.15 mg. of KCl, 0.32 mg. of $FeCl_3$ have been added, but even higher dilutions—0.03 mg. of $FeCl_3$ proved to be effective. The importance of these studies for the "Micrometabolism" (Wright[2]) in different diseases will be reported elsewhere.[4, 5] Anabolic and catabolic influences of drugs can easily be determined with these methods, *in vitro* as well as *in vivo*.

[1] Pribram, E., *Z. f. Kolloidchemie, Beih.*, 1911, **2**, 1.

[2] Wright, F., *Clin. Med. and Surg.*, 1933, **40**, 517.

[4] Pribram, *Arch. f. Gewerbepathologie*, 1934, **5**, 23.

[5] Pribram, *Schweizer. Wochenschr.*, 1934, in print.