THE INFLUENCE OF ADRENALIN, MODIFIED BY SALTS, ON THE BLOOD PRESSURE IN THE CAT.

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METHOD.

The usual procedure was employed in obtaining blood pressure records from the cat: the cannula was inserted into the carotid artery and connected to a mercury manometer; a saturated solution of sodium carbonate was used as a transmission fluid. In the first few experiments the test solutions were injected into the femoral vein with a hypodermic syringe, but because of the rapid clogging of the vessel from clotting as a result of this method, a glass cannula was tied into the vein and the injections made through this. The solutions were placed in the cannula and forced into the vein by compression of the attached rubber tube, after which the cannula was thoroughly washed to remove all traces of the substance used.

In preparing the salts for injection, volumetric solutions (molecular where the solubility permitted) of chemically pure substances were made, using doubly distilled water as a solvent. Before administration these were diluted to the desired concentration with doubly distilled water. The stock solution of adrenalin was made from Parke, Davis & Co.'s base — 1 mgm. to each cubic centimetre of water acidulated with 0.004 per cent hydrochloric acid — and was discarded when two weeks old. The dose given in each instance was 1 c.c. of the solution.

The effect of adrenalin on the cat. — When injected intravenously, adrenalin acts very quickly, a maximal rise in pressure taking place within a few seconds, succeeded by a return to normal in a few seconds more, the whole effect lasting on an average less than one minute. The after effect of fresh adrenalin is especially interesting: the curve does not stop when it has reached normal pressure after the rise, but
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continues to fall till the manometer has shown a decrease equal to or greater than the original rise (Fig. 1). I have been unable to find any such action recorded in literature dealing with adrenalin. Lohmann showed that, in certain admixtures of adrenalin and cholin, both substances might act separately, the adrenalin causing a rise in pressure followed by the cholin depression. To prove that such was not the case in these experiments the adrenalin was removed by oxidation; a 1:10,000 solution was made alkaline and allowed to stand for several days, when, upon delicate chemical tests, the adrenalin was found to be entirely absent; this solution after being neutralized produced upon injection neither a fall nor a rise in blood pressure, proving the absence of cholin as well as adrenalin.

The effect of salts with adrenalin.—The after effect of adrenalin caused me to look for a substance which, when injected simultaneously

Since this article was prepared for publication a similar finding has been recorded by v. Leersum: Archiv für die gesammte Physiologie, 1911, cxlii, pp. 377–395.


I have recently been informed by E. R. Weidlein that the methods at present in use for the purification of adrenalin are at fault, and that Parke, Davis & Co.’s crystalline adrenalin — considered 100 per cent pure by Schultz (Washington Hygienic Laboratory, 1910, Bulletin 61, p. 23)—really contains an impurity which may account for the after depression. Mr. Weidlein’s paper will appear shortly.

Parke, Davis & Co.
with it, might prevent the undesirable depression without in any way diminishing the initial rise produced by adrenalin. This substance was found in barium chlorid. In even as great dilution as a \( \frac{1}{128} \text{m} \) solution, barium chlorid injected alone will cause a marked stimulation of the heart action and a rise in blood pressure. When injected with adrenalin, the rise caused by the latter is noticeably augmented, the pressure does not fall so rapidly, and the after depression is entirely absent (Fig. 2). The strengthened heart beat may be observed for fifteen minutes or more after injection.

In order to determine whether the mere addition of a given amount of liquid (in these experiments 1 and 2 c.c.) to the circulation would in itself cause any change in pressure, several injections of Ringer’s solution were made and were found to produce no effect. The same statement holds true concerning the effect of Ringer’s solution on the change of pressure caused by adrenalin.

The next salt experimented with was sodium chlorid. Injection of an \( m/8 \) solution (which is of nearly physiological osmotic pressure) caused no change either in blood pressure or heart action, and an \( m/2 \) solution produced only a slight rise in blood pressure; these

\[ \text{NaCl, 0.7 per cent; CaCl}_2, \text{ 0.026 per cent; KCl, 0.03 per cent.} \]
results corroborate the findings of Hyde, Mayor, and Ritter. Nevertheless, from this work, sodium chlorid in the doses given may be considered a neutral salt. But when injected with adrenalin, it caused a decrease in the original rise; it did not, however, affect the length of action, nor did it prevent the after fall which usually follows the adrenalin rise.

Potassium chlorid in dilutions of \( m/32 \) may be considered practically neutral, both alone and in combination with adrenalin. Twice as concentrated solutions, however, have a depressing effect on blood pressure and heart rate when given alone (Fig. 3), and just the opposite effect in connection with adrenalin (Fig. 4). This latter result may be explained by the statement of Howell that potassium chlorid increases vagus irritability in certain doses, while in larger ones it depresses; the dose of potassium chlorid in connection with adrenalin was perhaps sufficient to depress the vagus, while alone it acted as a vagus stimulant, therefore slightly lowering the blood pressure.

Calcium chlorid and magnesium sulfate have a depressing effect on blood pressure, both when given alone and when administered with adrenalin. Meltzer and Auer obtained the same results from

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*HYDE: this Journal, 1908, xxiii, p. 201.
*MAYOR: Journal de physiologie, 1902, iv, 3, p. 425.
*RITTER: Deutsches Archiv für klinische Medizin, 1910, c, p. 11.
the injection of magnesium, but they used much larger doses, causing complete inhibition of the respiration as well as a fall in blood pressure.

Some experiments were undertaken with the phosphates as the result of a test which showed the adrenalin base to contain traces of these substances. The phosphates used were the acid, neutral, and alkaline sodium salts. No definite effect could be observed, either

when used alone or when given with adrenalin; the acid phosphate, however, increased the pressure somewhat, but had no effect on the adrenalin rise, while the neutral and alkaline salts were without effect when used alone, and only the alkaline one, Na₃PO₄, caused any change when given with adrenalin; the change produced here was a marked depression, sometimes even complete neutralization, of the adrenalin; but this was probably due to oxidation of the adrenalin (which takes place readily in an alkaline solution, see above) rather than to any specific effect of the tri-sodium phosphate itself.

Another substance which, being a waste product in the body, and hence normally coming into contact with other constituents of the blood, would be of interest in this connection, is the purin derivative, uric acid. This compound alone causes a decided rise in mammalian blood pressure; its effect on heart action, however, is very insignificant, being in a majority of cases quite neutral, in others causing only a slight increase in heart rate. It exhibits a peculiarity when injected with adrenalin in that it causes a decrease in the normal adrenalin rise. Just why this seemingly paradoxical result should follow the combination of these two body products will probably not be understood until the action within the body of certain substances produced in normal metabolism upon the internal secretions, individually and in co-operation with each other, is better known.

Control injections of hydrochloric acid and sodium hydroxid of equal acidity and alkalinity to that of m/16 NaH₂PO₄ and Na₃PO₄,
respectively, showed that the results obtained from these salts were not due to their reactions. The hydrochloric acid caused a slight depression, while the sodium hydrate had practically no effect upon the blood pressure. Acid solutions equal in strength to the acidity of 1:10,000 adrenalin had no effect whatever; an alkaline solution of equimolecular concentration was also neutral.

This work was done at the suggestion of Dr. Ida H. Hyde, for whose valuable aid I am much indebted.

**CONCLUSIONS.**

1. Adrenalin has an undesirable after-depressing effect on mammalian (cat) blood pressure. This may be due to a hitherto unsuspected impurity, as suggested by Weidlein. The after effect may be counteracted by very small doses of barium chlorid. Barium chlorid also strengthens heart action and sustains high blood pressure for some time.

2. The waste product, uric acid, antagonizes adrenalin pressure, although alone it increases blood pressure.

3. The salts which cause a rise in pressure are: NaCl, m/2; BaCl₂, m/128 and m/32; uric acid; and NaH₂PO₄, m/16. Those lowering the pressure are: KCl, m/16 and m/32; CaCl₂, m/16; and MgSO₄, m/8. Those which show no definite action: Ringer's solution; NaCl, m/8; CaCl₂, m/32; and Na₂HPO₄, m/16.

4. Adrenalin pressure is augmented by: BaCl₂, m/128 and m/32; KCl, m/16. Salts which depress the effect of adrenalin are: NaCl, m/2; CaCl₂, m/16; MgSO₄, m/8; and uric acid.