

groups of workers is still obscure. The problem of the part played by the adrenal medulla in water metabolism under normal conditions is one of considerable importance and the finding reported here that small doses of dl-nor-epinephrine stimulate water diuresis without giving other gross overdosage effects makes it feasible to seek further for evidence of a physiological role for the adrenal medulla in such processes. We intend to explore such possibilities in extension of this work by attempting an analysis of these actions of nor-epinephrine in terms of circulatory and renal mechanisms. It is pertinent to point out that the lack of gross overdosage effects with dl-nor-epinephrine may be due to the lesser toxicity of nor-epinephrine as compared with epinephrine(8).

It is well established that dibenamine will block and often reverse some of the actions of epinephrine(12). This proved to be the case in our experiments for adrenalin but a reversal effect was not seen with nor-epinephrine. In other words, in the intact rat, dibenamine more effectively blocks the action of injected adrenalin than it does nor-epinephrine. However, in the absence of the

adrenal medulla dibenamine does not have any blocking action on nor-epinephrine and its characteristic water retaining properties are absent. It is possible that the blocking action of dibenamine on water diuresis is dependent upon the presence of either endogenous or administered medullary epinephrine. It would be of interest to see if this holds true for other types of dibenamine blockage.

Summary. The injection of non-epinephrine in the rat is more effective in causing an augmentation of water diuresis than is adrenalin. Pure l-epinephrine has no stimulating action on diuresis.

Dibenamine causes a water retention in intact rats but fails to do so in adrenal medullectomized rats.

Dibenamine blocks and reverses the diuretic activity of adrenalin in intact rats but it less effectively blocks such activity of nor-epinephrine. Dibenamine, in the dosage used, was incapable of blocking the action of nor-epinephrine in medullectomized animals.

These results indicate that the diuretic action of adrenal medullary hormone is not due to epinephrine but to the presence of nor-epinephrine.

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Influence of Blood Incompatibilities on Measurement of Blood Volume by Cell-Tagging Methods.* (18100)

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During a recent series of direct comparisons in dogs of blood volume determined with radio iron (Fe^{55}), CO and dye (T-1824)(1),

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we sometimes encountered reactions to the injections of donor blood. In one dog the reactions were so severe that the tests were discontinued. In a second animal with very severe reactions we decided to complete the test and then found that both the CO volume, which normally agrees with the dye-volume, and the radio-iron volume were extremely low as compared with the results of the dye determination. Subsequently, we noted that if the blood for CO saturation and injection was drawn from the recipient dog itself in-

stead of from the donor, reactions to the injection occurred less frequently and the agreement in volume measured with CO and dye was more consistent. Yet the ratio of blood volume measured by radio iron and by dye still revealed large fluctuations (0.7 to 1.0). These and other observations led us to investigate the effect of blood incompatibilities on the blood volume measurements.

The cross-matching was performed according to the procedures developed by Dr. Angie Hamilton of Philadelphia(2). In tests on the dogs still available from earlier experiments it was found that the experiments in which the iron values were low relative to dye or CO values were those in which the iron donor cells showed clumping reactions in the recipient dog's serum.

In order to explore this matter further the blood volume of the same dog was measured in successive tests with matching and non-matching donor bloods. Where matching was satisfactory and the dog showed no overt reactions to the donor bloods, the values from the different methods agreed fairly well. Where either the radio iron or CO donor cells showed incompatibility in the recipient's serum, the recipient had definite reactions (one animal died in shock 3 hours after the injections) and the radio-iron volume and/or CO volume were low compared with the dye-volume. However in these repeated tests the total blood volume by the dye method was nearly the same whether or not reactions were present, thus indicating that the iron and CO measurements were the ones most affected by the untoward reactions.

These observations suggest that when the cells are clumped in the reactions of incompatibility the tagged cells may not be distributed evenly throughout the circulation, especially in the small vessels, and that under these circumstances a cell-tagging method may

underestimate the volume.

The literature fails to reveal that any attention has been paid to the question of blood matching in blood volume determinations in dogs. In experiments on man with radio iron or with the Ashby marked cell method, universal donors are used. Yet careful observers report the occurrence of occasional reactions(3). The P^{32} method(4,5), seemingly eliminates the problem of blood incompatibilities. However, a few preliminary tests have given indication that dog blood after incubation with P^{32} , and occasionally after saturation with CO, shows slowly appearing clumping reactions with fresh serum from the same animal.

The possible effect of these factors on the measurement of blood volume with various cell-tagging methods are being studied in more detail.

Summary. A study of the blood volume of the dog as measured simultaneously by the Dye T-1824, by carbon monoxide and by radioactive iron, Fe^{55} , has shown that the values measured by the cell-tagging methods are distinctly lower than the value given by the dye method whenever the donor blood tagged with CO or Fe^{55} shows incompatibility with the blood of the recipient animal. However, when the bloods of the donor and the recipient animals show no incompatibility, the results by the three methods show improved agreement. These results suggest that the cell-clumpings occurring in the reaction of incompatibility, by making the smaller vessels inaccessible to the clumped cells, reduce the volume measured by the tagged cells.

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