mals, without exception, in attempting to move walked backward. After the bandage was removed they immediately returned to the normal method of progression. Such test could be performed repeatedly on the same animal with similar results.

To determine whether this retrogression was not due to voluntary movements of the nature of escape reaction, we performed these tests on the decerebrated fowl. The results were the same as in normal animals, indicating that this phenomenon is of a reflex nature (forced movement).

We conclude, therefore, that normal progression in the chicken is dependent upon the posture of the neck, or the tonic state of the neck muscles. This ability is lost as soon as the posture of the neck is changed (neck ventroflexed upon the trunk), and progression is replaced by retrogression.

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On the existence of a pressor substance in the blood of clinical cases of hypertension.

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It is common knowledge that neither the etiology nor the pathogenesis of hypertension is understood. In a rather loose way it has been correlated with diseases of the arteries and kidneys. Whether the reduction in the cross sectional area of the vascular bed is due to anatomical changes in these structures, or to some chemical substance circulating in the blood, which is capable of exerting a pressor response, has never been answered adequately.

We have, therefore, attacked the problem by transfusing the unchanged blood of patients with hypertension into animals, in order to see whether a pressor response could be detected in the animals so treated. In such a case the theory of the reduction of the peripheral vascular bed as the primary cause of hypertension could be excluded. Likewise the hypothesis of Hülse[1] regard-

[1] Hülse, *Z. ges. Exp. Med.*, 1922, xxx, 240 and 268.

ing vascular hyperirritability would have to enter into serious consideration in the explanation of the genesis of high blood pressure.

The search for pressor substances in the blood is by no means new. Very soon after the development of the studies on epinephrin the idea naturally suggested itself that this substance which exists in the blood normally, because of its blood pressure raising influence, would be found in excess in cases of hypertension. This seemed particularly likely in view of the pathological reports that medullary hypertrophy or tumors of the suprarenal gland had been found in association with hypertension. That these findings were only chance occurrences was proved by their presence without hypertension, and conversely, hypertension without suprarenal hyperplasia. Bröking and Trendelenburg, [2] and Stewart [3] tested for adrenalin in cases of hypertension with negative results. They admit the crudeness of the methods used for the detection of these substances.

Exper. 1.—Varying amounts of physiological saline, from two to twenty cc. were injected into the veins of a cat. In each case a small rise of pressure occurred. The effects on blood pressure, of the smallest and the largest dose, were equal.

Exper. 2.—20 cc. of homologous fresh blood were transfused into a cat. The immediate, small rise in blood pressure was similar to that resulting from the injection of the same amount of saline.

Exper. 3.—12 cc. of rabbits' whole blood transfused into a cat produced the usual initial volume effect on the blood pressure followed by a marked fall. This depressor effect will be explained later.

Exper. 4 and 5.—12 and 16 cc. of unchanged human blood taken from two women with normal arterial pressures were transfused into two separate cats. In each case there resulted the slight initial rise due to the volume injected.

Exper. 6.—20 cc. of human blood from a case of hypertension were transfused into an animal (cat). The usual short primary rise was followed by a prolonged great secondary rise in the mean, systolic, diastolic and pulse pressure, together with a slowing of the heart rate.

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[2] Bröking and Trendelenburg, *Deutsche Arch. f. klin. Med.*, 1911, ciii, 168.

[3] Stewart, *J. Exp. Med.*, 1911, xiv, 377.

Exper. 7.—In another cat the injection of 18 cc. of the same patient's blood produced the same initial rise in blood pressure. The secondary effect was the mirror image of the first one—a marked dropping in pressure with cardiac slowing resulted. This depressor and bradycardic effects were only to be interpreted after the subsequent experiments were performed.

Exper. 8.—18 cc. of whole blood from a clinical case of hypertension was transfused into a cat. The insignificant primary rise followed by a marked fall in pressure, accompanied with a slow large pulse pressure oscillations, followed. This secondary effect is clearly of vagus origin as was shown in the next experiment, No. 9, where the same procedure was carried out on an atropinized animal. Here there was no depressor effect. In the following experiment, No. 10, which was a repetition of 9, atropine not only prevented the secondary drop in blood pressure, but also allowed the secondary pressor effect to make itself manifest. In the latter case there was no increase in pulse pressure.

Exper. 11.—12 cc. blood of another woman with hypertension were transfused into a unatropinized cat. There occurred a very marked, prolonged rise, followed by a very pronounced fall in blood pressure and disappearance of pulse pressure, both of which gradually rose and were later followed by a bradycardia. Here again we see a pressor effect, followed by a depressor (Vagus) phase.

Exper. 12.—An alcoholic extract of the blood of a hypertensive (case used in Exper. 8-9-10) was made, dissolved in water. Ten cc. were injected into the vein of a cat whose vagi were unaffected. An immediate drop in pressure and slowing of the heart occurred. The depressor effect was so powerful that it overshadowed even the primary volume effect. When this extract was diluted five times and 10 cc. infused into the cat's vein (Exper. 13) both a primary and secondary rise of blood pressure occurred very similar to the effect of unchanged blood from the same patient.

It is obvious that we are dealing in the blood mixture with two substances, a depressor substance which was present in most of the cases of heterologous blood injected, and a pressor substance. That the former was probably protein in nature, and the reaction was anaphylactic in character, seemed quite probable.

To test this 1 cc. of horse serum was injected into the vein of

a cat and produced the expected depressor and bradycardic (Vagus) effect (Exper. 14).

In Exper. 15 an attempt was made to desensitize the cat against the specific protein (horse-serum) by injecting the latter, diluted and in small amounts, into the vein before the large amount of concentrated protein was given. The latter then had only a very slight depressor effect, which would not interfere seriously with our experiments. The animal could in a similar manner be desensitized against an alcoholic extract of rabbits' blood. (Exper. 16).

Exper. 17.—Cat was vagotomized on both sides to eliminate the vagus effect and desensitized in the usual way against human blood from a clinical case of hypertension (same case as in Exper. 8-9-10). Now 18 cc. of unchanged blood of this patient were transfused into the cat. A negligable primary effect but a very striking secondary effect occurred. This had the usual delay, but the pressor effect was greater than in any of our previous experiments. Apparently the method of desensitization and vagus exclusion allowed the pressor effect to unfold itself in bold relief.

Exper. 18.—Eighteen cc. of the same blood were injected into a cat with intact vagi but desensitized by the previous injection of 4 cc. of the same blood subjectaneously. A very pronounced primary rise in blood pressure occurred. This curve was checked against that produced by varying amounts of epinephrin, and corresponded very closely with the curve obtained from the injection of .5 cc. epiniphrin 1-1000 dissolved in 19:5 cc. of normal saline. The pressor substance may thus be expressed in terms of epiniphrin units.

Exper. 19.—10 cc. of blood cells of a case of hypertension were injected into the vein of a cat and a delayed though marked pressor effect was observed.

CONCLUSIONS.

1. Blood from cases of hypertension contains a pressor substance.

2. The blood proteins by virtue of their anaphylactic reaction and the intact vagi of the experimental animals inhibit the otherwise obvious pressor response. Hence these factors should be eliminated in such experiments.

3. No pressor effect of any kind was ever seen by us from the injections of comparable amounts of saline, rabbits' blood or human blood of people with normal blood pressures.