PROCEEDINGS

OF THE

PHYSIOLOGICAL SOCIETY,

1894. No. I.

UNIVERSITY COLLEGE, LONDON. *March 10th.*

On the Physiological Action of Extract of the Suprarenal Capsules.

G. OLIVER and E. A. SCHÄFER, F.R.S. brought forward the following communication :—

The suprarenal capsules yield to water (cold or hot), to alcohol or to glycerine a substance which exerts a most powerful action upon the blood vessels, upon the heart, and upon the skeletal muscles. These effects have been investigated upon the dog, cat, rabbit and frog. In the frog the solutions were injected into the dorsal lymph-sac, in the rabbit subcutaneously and into a vein, in the other animals into a vein. The alcohol extracts were first dried and the residue extracted with normal saline; the watery decoctions were made with normal saline, and the glycerine extracts were largely diluted with the same previous to injection. The doses employed have varied from a mere trace up to an amount of extract equivalent to 3 grains (0·2 gramme) of the fresh gland; in one or two instances we have given larger doses with the object of obtaining if possible a lethal result. The extracts used have been made from the suprarenals of the calf, sheep and dog. Exactly similar effects have been obtained in each case. Except in the case of the frog we have not obtained any marked effect from subcutaneous injections of comparatively small doses. We are, however, able to confirm the statement of Foa and Pellacani that hypodermic injections of the aqueous extract produce death in 24 hours in the rabbit; but a large dose, equal to 50 grs. of the gland, was necessary. Even after intravenous injection the symptoms entirely pass off after a few minutes, showing that the poison must be rapidly eliminated.

The effect upon the blood vessels is to cause extreme contraction of the arteries, so that the blood-pressure is enormously raised. This is most evident when the vagi are cut in order to obviate the inhibitory action upon the heart which otherwise occurs; it is also seen after section of the cervical cord. The blood-pressure may rise from 2 to 4 times above normal. This extreme contraction of the vessels is evidenced by the plethysmograph; section of the nerves going to the limb produces no difference in the result[1]. The effect is therefore peripheral. This can also be shown in the frog with its nerve-centres destroyed, and through the blood vessels of which normal saline is allowed to circulate; if only a small quantity of suprarenal extract is added to the saline the flow almost entirely ceases.

The time which elapses between the injection into a vein and the first effect upon the blood vessels is in the dog from 25 to 30 seconds. But if an experiment has been conducted for some three hours or more, the animal during the whole of this time having been under the influence of morphia and curare, the contraction of the vessels of a limb is preceded by a preliminary expansion, the cause of which is as yet not clear. It is however a constant phenomenon.

Traube's curves are abolished during the greater part of the time that the substance is producing its effect upon the vessels. The effect on the heart, as long as one vagus remains uncut, is to produce powerful inhibition. During this time the auricles may come to a complete standstill, the ventricles continuing to beat with a slow independent rhythm. But if both vagi are cut the heart-beat becomes greatly accelerated (to twice its former rate) and also augmented; the augmentation showing itself most markedly upon the auricular tracing. The latency of this augmented action of the heart is less than that of the vascular contraction. So far as we are able to judge from one or two experiments which were kindly made for us by Dr Sidney Ringer, the direct action of the drug upon the frog ventricle as recorded in a Roy tonometer does not appear to be marked. When added to the circulating fluid used for perfusion the extract produced only a slight increase in the strength of the beat, and even this was not maintained.

The effect upon the skeletal muscles has been investigated in the frog. The movements of a frog to which a hypodermic injection of extract of suprarenal capsule (equal to 1 or 2 grains of the fresh gland)

[1] This is the rule, but we have had one notable exception in which in the earlier part of the experiment the limb, the nerves of which were cut, showed a large expansion. After a short time, however, this passed off and the limbs gave similar curves.

have been given soon become slow, and after about half-an-hour the reflexes are very faint and almost abolished; the animal soon appears completely paralysed. The muscles however still contract on being stimulated, either directly or through the motor nerves, but the contractions are modified, the relaxation period being greatly prolonged, as with veratria poisoning. The period of latent stimulation is not greatly, if at all, lengthened. The fatigue curves were rapidly developed. The effect is not at all comparable to that produced by curare.

We have noticed a slight effect to be produced upon the respiration, which may become shallower; but in the doses we have used the result was very slight when compared with the prodigious effects upon the heart and blood vessels which were obtained.

Although poisonous effects resulting from hypodermic or intravenous injections of extract of suprarenal capsules have been mentioned by more than one previous observer, we have not been able to find any record of experiments tending to show exactly what organs were affected, nor do such symptoms as have been described by others agree in most respects with the changes we have here recorded. As to the chemical nature of the active substance we are unable at present to make any positive statement, since the process of isolating such a body in a fairly pure condition is necessarily slow and difficult. We are, however, able to make the negative affirmation that it is not neurin, although neurin has by more than one observer been conjectured to be the active agent in such extract. For the symptoms produced by neurin do not in any way agree with those produced by the active substance in our extract; this we are able to affirm, both from the careful work regarding the physiological action of neurin which has been done by Cervello, and also by determining for ourselves by the same methods as we have employed in investigating the suprarenal extract what is the action of neurin upon the several organs. Suffice it to say that the most prominent effect produced by neurin is paralysis of the respiration. The effects upon the heart and vessels are relatively slight, and, such as they are, are quite different from suprarenal extract. We have also investigated the action of the salts of neurine (phosphate, hydrochlorate) and have obtained exactly the same results as with the base itself. We are unable to confirm the statement of Marino-Zuco that the addition of either mineral acid or a base to suprarenal extract abolishes its toxic properties (which he ascribes to the presence of phosphate or glycerophosphate of neurine).

We are indebted to Mr Moore for the preparations of neurine

which we have used, and for much other help in the chemical part of the investigation, and to Messrs Willows, Francis and Butler for a large supply of glycerine extract and alcohol extract of calf suprarenals, which they have been at much trouble to prepare specially for this work. We have also tested the effect of a clear watery extract obtained from Paris (in a sealed tube) and furnished to us by the kindness of Dr Hale White.

The physiological effect of this solution, as to the mode of preparation of which we are wholly ignorant, proved to be precisely the same as that of our own extracts.

The above communication was illustrated by two experiments, as well as by numerous tracings and photographs of tracings.

The Structure of the Fovea centralis.

C. H. GOLDING BIRD and E. A. SCHÄFER, F.R.S. showed preparations and sections through the fovea centralis of the human retina in which the following points were rendered evident:—

1. Besides the dipping of the limitans interna which constitutes the fovea proper, there exists a well-marked dipping inwards of the limitans externa, forming what may be termed an external fovea.

2. The cone-nuclei at the fovea are not, as is usually represented, closely applied to the limitans externa, but gradually leave that layer, as the centre of the fovea is approached, the part of the cone-cell between the cone proper and the cone nucleus becoming more and more elongated, until at the very centre of the fovea the nucleated part of the cone-cell is almost, or entirely, sessile upon the external molecular layer.

3. The inner granules (bipolars) are not wholly absent even at the centre of the fovea.

4. The nerve-cells are not oval bipolar structures such as are usually represented in this part, but are rounded bodies with their peripherally directed process passing vertically into the inner molecular layer, as in other regions of the retina. The layer of nerve-cells ceases a short distance from the centre of the fovea, but one or two isolated cells of similar character may be found even close to the centre.

On Nucleo-albumins.

W. D. HALLIBURTON, F.R.S., and T. G. BRODIE stated that they had continued their investigations on the properties of nucleo-albumins during the past year. They had previously found that intravascular

coagulation is produced not only by Wooldridge's nucleo-albumins (prepared by the addition of weak acetic acid to an aqueous extract of organs like the thymus), but also by nucleo-albumins prepared by another method, which may be briefly termed the sodium chloride method. They confirmed Wooldridge's statement that this power is lost after repeated solution and reprecipitation by means of dilute solution of sodium carbonate, and acetic acid respectively, and had found also that repeated alternate treatment of the nucleo-albumin (prepared by the sodium chloride method) with sodium chloride and water produces a similar loss of power. It is this last point, the explanation of which they had been seeking during the past year. Their investigations were not yet completed, but so far as their experiments (with the thymus gland) had at present gone, the cause of the loss of coagulative power appears to be due to a removal of the nuclein from the nucleo-albumin by the repeated use of sodium chloride. The percentage of phosphorus varied from 0·57 in the most active preparation, to 0·094 in the least active. This could not be due to diminution in the quantity of lecithin, as all the preparations had been thoroughly extracted with alcohol before the quantitative analysis was made.

Further experiments upon the reaction of the developing Chick to changes of temperature.

M. S. PEMBREY and M. H. GORDON, made the following communication:—

In a communication given at the Meeting of the Physiological Society at Oxford, July 8th, 1893, we described the preliminary results of an investigation upon the reaction of the developing chick to changes of temperature. We now wish to give some further results.

The measure employed to test the reaction is the discharge of carbonic acid. The apparatus for the determination of the respiratory exchange is similar to that used by one of us for investigating the reaction-time of mammals to changes in the temperature of their surroundings.

The main results obtained at present show that during the greater part of the period of incubation the developing chick reacts as a cold-blooded animal; a rise in the external temperature increases, a fall of temperature diminishes the amount of carbonic acid discharged. The reaction shows a marked latency of about 30 minutes. The following figures may be given as examples:—

Egg V. on 16th day of Incubation.

Consecutive periods of thirty minutes.

Experiment	Temperature of bath	CO_2 discharged grs.
1	39°·5	·0141 ·0141
2	39°	·0133 ·0133
3	25°	·0113
4	25°	·0090
5	38°	·0082
6	37°	·0089
7	38°	·2669 (11 hrs.) [·0120]

Egg V. on 18th day of Incubation.

Consecutive periods of thirty minutes.

Experiment	Temperature of bath	CO_2 discharged grs.
1	38°·5	·0112
2	25°	·0109
3	38°·5	·0047
4	38°·5	·0082
5	38°·5	·0107
6	38°·5	·0103
7	38°·5	·0117

Towards the end of incubation the developing chick appears to pass through a neutral stage, during which a rise or fall of temperature shows no marked effect upon the carbonic acid. The following Table is given as an example:—

Egg IV. on 21st day of Incubation.

At the beginning of the experiment there was a hole half an inch square in the egg; the chick could be seen moving about; it also put its beak out of the hole.

The following determinations are consecutive periods of fifteen minutes' duration:—

Experiment	Temperature of bath	CO_2 discharged grs.
1	37°·5	·0122
2	38°	·0138
3	24°	·0125
4	24°	·0120
5	36°	·0127
6	37°·5	·0146
7	38°	·0153
8	38°·25	·0147
	—	·0148
	—	·0148
9	38°·5	·0151
	—	·0152
10	24°	·0169
	—	·0169
11	24°	·0145
	—	·0144

At the end of the experiment the chick was curled up in the egg; it chirped lustily.

The following experiment was now made upon a developing chick in Egg IX., on the 21st day of incubation. The chick within the egg was first shown to be in this apparently neutral stage; it was then taken out of the egg by enlarging the hole, which the chick itself had made. The premature chick was now exposed to changes of temperature as before, the determination of the carbonic acid showed that it reacted as a cold-blooded animal. The chick became very feeble and was unable to stand. It was therefore placed in the warm incubator and kept there all night. The next morning it had recovered and appeared quite well. Its reaction to changes of temperature was tested and it was found to react as a warm-blooded animal. Within thirty minutes the carbonic acid was increased from ·0195 grm. to ·0282 grm.; by a fall in temperature from 37° to 23° C.

Several other experiments showed that the recently hatched chick when in a healthy condition reacted to changes of temperature in a manner similar to that of warm-blooded animals.

These experiments are being continued to obtain further confirmation, and to find out, if possible, the important factor in the change from the cold-blooded to the neutral stage, and from that to the warm-blooded condition. The experiments, especially the effect of shock, lead us to believe that the activity of the neuro-muscular system is the important factor.

The Reaction-time of the Frog to changes of temperature.

By M. S. PEMBREY.

(*Preliminary Note.*)

During the winter of 1893—94 experiments have been made on the reaction of the common frog to changes of temperature, and it has been found that, on raising the temperature from 9° C. to 19° or 20°, no increase is obtained in the carbonic acid discharged in consecutive periods. If, however, the temperature be raised a degree or two above 20° there is observed a marked and often sudden increase. The following results are for consecutive periods of twenty minutes. The experiments were all made upon one frog:—

Experiment	Temperature of bath	Carbonic Acid discharged
I.—13–xii–93	11°·75	·0013
	11°·75	·0008
	20°	·0011
	19°	·0008
II.—13–xii–93	9°	·0007
	10°	·0008
	20°	·0009
	20°·5	·0009
	20°	·0008
III.—15–xii–93	10°·25	·0006
	10°·75	·0006
	24°	·0006
	23°	·0024
	22°	·0017
	10°·75	·0011
V.—17–xii–93	11°·5	·0008
	11°·5	·0007
	25°	·0008
	23°·25	·0014
VIII.—1–i–94	10°·75	·0007
	11°	·0007
	19°·75	·0005
	20°	·0007
	19°·5	·0008
X.—3–i–94	9°·25	·0005
	9°·25	·0005
	15°·75	·0006
	15°·5	·0007

Experiments of longer duration and also the records of the temperature of the frog show that these results are not due solely to latency.