from the horse. The tubes which came from the sensitized individuals presented a distinct response upon the addition of minute amounts of horse serum, while the controls failed to respond even on the addition of large amounts of horse serum. The contractile response, although much less pronounced than in the case of the guinea-pig, is still unmistakable. The response to ergamine, adrenalin, and other similar drugs, is also very much less marked, in the case of the human preparation. From an anaphylactic standpoint, the human smooth muscle is, therefore, intermediate between that of the guinea-pig and that of the rabbit. This fact explains the character of the anaphylactic symptoms which have been observed in human beings.

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The cerebellum in cases of lowered blood pressure and "shock," an experimental study.

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The concept of the histology of the Purkinje cell held today by many neuropathologists is but slightly if at all advanced beyond the classification enunciated by Nissl in 1897.

As an introduction to the following work it was necessary to make an investigation of the Purkinje cell in normal animals employing different methods of fixation and staining. It seems desirable therefore not only to state my own views as to classification but also to briefly outline the technique used.

Although monkeys (*Macacus rhesus*), rabbits, cats and dogs were used in this histological study yet the conclusions in this presentation are drawn altogether from the dog.

The animals were all well fed and young. No animal was used which was not in good health. Care was taken to exclude the factor of physical exhaustion. No animal was brought in a shrinking or terrified condition to the operating room. When

everything was ready the dog was quickly overcome with either chloroform or ether.

As soon as the anesthesia was complete the thorax was opened rapidly and a canula introduced into the descending aorta, pointing upward. The right side of the heart was then opened and two liters of Ringer's solution were allowed to flow through the canula. After the Ringer's solution fixation was secured either by Zenker's fluid or by 10 per cent. formaldehyde solution. Followning this the brain was at once removed and placed in Zenker's fluid or 10 per cent. formaldehyde, corresponding to the fixative used for perfusion.

Tissue was mounted both in celloidin and paraffine and stained by many methods. This report is based on the following methods: Eosin-Unna's alkaline methylene blue, the carbol-thionin, Mallory's aniline blue and the hemalum-acid fuchsin. In most cases blocks of tissue were cut so that the Purkinje cell might be studied in three planes.

In describing the following types of Purkinje cells it were well to call attention to some characteristics common to all and also to accentuate the fact that I do not claim that these types represent essentially different entities. This may be so, or on the other hand the different types may represent different stages in metabolic activity of a single entity.

CHARACTERISTICS COMMON TO ALL TYPES OF PURKINJE CELLS.

1. The nucleus is usually oval and its long axis does not necessarily correspond to the long axis of the perikaryon.

2. Excentric placing of the nucleus is found frequently in cells which we must accept as normal.

3. The nuclear cap is a condensation of tigroid material in the form of a crescent which is applied so closely to the nucleus that at times it is difficult to say whether the substance be intra or extranuclear. The periphery of the cap is smooth in the majority of cases. But occasionally a lumpy or torn appearance is found in which event ragged masses of the cap project into the cytoplasm. The nuclear cap stains intensely with the basic dies.

4. The periphery of the nucleus is not necessarily an unbroken oval or circle. In conditions which we must accept as normal

there are frequently found instances of irregularity in nuclear contour. These may amount at times to angular indentations.

5. The nucleolus stains intensely basically but differs somewhat in tint from the chromatin or tigroid substance in that with thionin it appears distinctly a bluish dark blue while the chromatin and tigroid substance with the same stain are of a purple tint.

6. The staining of the primary dendritic trunk is variable in all the types. At times the trunk may be followed easily to its first or second divisions. But in other cells just as normal there is only a very faint indication of the trunk.

TYPES OF THE PURKINJE CELL IN THE DOG.[1]

Type α.—The perikaryon is 25 μ wide and 34 μ long. The nucleus has a mean diameter of 12 μ. The nucleus shows a small amount of chromatin irregularly distributed. The cytoplasm shows a moderate amount of tigroid substance on a light background. This tigroid substance is not arranged as in the anterior cornual cells. The masses are quite irregular in shape and in distribution. Part of the cytoplasm may show little of this substance while in another locality it may be dense.

Type β.—The perikaryon is 22 μ wide and 32 μ long. The nucleus has a mean diameter of 10 μ. Both nucleus and cytoplasm show a dark background. There is about as much chromatin in the nucleus as there is tigroid substance in a field of equal area in the cytoplasm. The arrangement of the tigroid substance is more uniform than in type α.

Type γ.—The perikaryon is 30 μ wide and 35 μ long. The nucleus has a mean diameter of 12 μ. The nucleus shows a small amount of chromatin, irregularly distributed. The cytoplasm has a light background. The tigroid substance is moderate in amount and distributed in a fairly regular manner through the cytoplasm. On account of the moderate amount of tigroid substance the color tone of the cell is light and the nuclear cap stands out in bold relief.

Type δ.—The perikaryon is 30 μ wide and 35 μ long. The nucleus has a mean diameter of 12 μ. The nucleus shows as

[1] The measurements are in all cases approximate only, and are given simply as a guide to those not already familiar with the histology of the Purkinje cell.

small an amount of chromatin as in type γ. The cytoplasm shows a very scant amount of tigroid substance which is distributed with moderate regularity. The granules of tigroid substance are so fine and so few that the cell appears very pale and with too much lighting from the substage may even be missed in a careless examination. At times there is noted near the periphery a thread-like formation of the tigroid substance. In this case the threads run concentrically with the periphery of the perikaryon.

Type ϵ.—The perikaryon is 28 μ wide and 38 μ long. The nucleus has a mean diameter of 12 μ. The nucleus is as in type γ. The tigroid substance is of about the same density as in type γ but the arrangement is peculiar in that the cell appears as if there were an exoplasm and an endoplasm, both clearly defined, and the tigroid substance limited to the latter.

Type ζ.—The perikaryon is 14 μ wide and 45 μ long. The nucleus has a mean diameter of 7 μ. The nucleus and cytoplasm are similar to type β. The cell is often extremely pyknomorphous, even in thin sections. One often finds this type of cell bent almost at right angles or irregularly twisted.

Type η.—The perikaryon is almost circular with a diameter of 15 μ. The nucleus has a mean diameter of 8 μ. The nucleus and cytoplasm appear as in type ζ.

Type θ.—This type of cell is much broader than it is long. It is a very infrequent finding and so far as its staining characteristics are concerned it usually approaches type β.

If one follow the granulo-molecular junction through many folia it becomes evident that there is no definite choice or arrangement of these several types of cells. A succession of from four to ten or twelve type δ cells is a frequent occurrence. To either side of this collection may be found cells of type β. The absence of Purkinje cells over long extents of granulo-molecular junction is of irregular but normal occurrence and is found as frequently at the apex of a folium as in the deep recess of a sulcus.

CLASSIFICATION OF EXPERIMENTAL WORK.

Our animals were subjected to conditions which reduced the blood-pressure markedly for a period of two hours. Moreover in

order to test the theory of possible transmission of centripetal impulses from the periphery to the central nervous system during full anesthesia certain means as noted below were used over prolonged periods. The details of these experiments I shall leave to Dr. Jackson and Dr. Janeway to describe.

In all twenty-two dogs were used. The experiments may be divided into five series, as follows:

Series 1.—Vena cava occlusion and stimulation of both sciatics.

Series 2.—Hemorrhage.

Series 3.—Handling intestines.

Series 4.—Transection of mid-brain anterior to the corpora quadrigemina and handling of intestines.

Series 5.—Transection of mid-brain and stimulation of sciatics.

In series 1 there were thirteen dogs; in series 2 there were four dogs; in series 3 there were two dogs; in series 4 there were two dogs and in series 5 there was one dog.

In the thirteen dogs of series 1 the blood-pressure averaged during the experiment from 34 to 52 mm. The lowest pressure recorded was 20 mm. which was noted in three cases; the highest pressure recorded during these experiments was 70 mm. which was noted in three cases. Eight of the animals in series 1 were killed immediately at the end of the experiment. Two animals were killed six hours after the experiment. One animal was killed five and one half hours after the experiment and two were killed twenty hours after.

In the four dogs of series 2 the average blood-pressure recorded during the experiment was from 34 mm. to 54 mm. The lowest pressure was 20 mm. and the highest 70 mm. All the animals of this series were killed at the conclusion of the experiment.

In the two dogs of series 3 the blood-pressures were in one 150 mm. at the beginning of the experiment and 60 mm. at the end; in the other animal the pressure was 130 mm. at the beginning and 90 mm. at the end. Both dogs were killed at the end of the experiment.

In the two dogs of series 4 the blood-pressure was 80 mm. at the beginning and 30 mm. at the end in one; and 80 mm. at the beginning and 70 mm. at the end in the other. Both animals were killed at the termination of the experiment.

The one dog of series 5 was killed at the end of the experiment. The blood-pressure was not recorded.

RESULTS OF THE MICROSCOPICAL EXAMINATION OF THE CEREBELLA IN THE FIVE SERIES.

I would say that owing to a mistake on my part three of the brains were perfused by a solution of formaldehyde of only a little over 1 per cent. and afterward placed in this weak fixative, I thinking that 10 per cent. had been ordered. These specimens were two in series 1 (S. 155 & S. 158) and one in series 3 (P. 3). These specimens must be discarded from any consideration as post-mortem change is quite evident. In series 1, one specimen (S. 212) has been over differentiated so that new material will have to be prepared before judgment can be passed as to the condition of the Purkinje cells.

This leaves ten specimens in series 1 (S. 140, S. 145, S. 150, P. 1, S. 171, S. 176, S. 184, S. 187, S. 213, and S. 218) on which I would report as follows:

In specimen S. 218 the Purkinje cells show a much greater percentage of type β cell than is normally found. Moreover the pyknomorphous cell predominates. What is possibly furthest from normal is a pronounced vacuolization which one finds in these sections more than occasionally.

It will be noted that the dog of this experiment was not killed until 20 hours after the completion of the work. This is a factor which can not be set aside.

All of the other specimens of this series can be pronounced normal. I would call attention to the gross appearance of the staining in P. 1, which shows well the deeper staining of the paraflocular granules than elsewhere in the cerebellum. This is a normal finding.

In series 2 the following report can be made:—

P. 9 appears normal. This animal's blood-pressure was from 20 mm. to 40 mm. S. 219 appears normal. The blood-pressure in this case was 50 mm. to 70 mm. P. 5 appears normal. The blood-pressure was 25 mm. to 40 mm. Concerning P. 4, Dr. Jackson records on the chart: "Poor transfusion." But this can

not account for the cell picture seen in this case. There are very few type α cells. The number of pyknomorphous cells is very large, as is also the number of type ϵ cells. Very pronounced vacuolization is frequently found. Comparing the sections of this animal with those of others, normal and abnormal, there are noticeably fewer Purkinje cells in P. 4. Of course this can not be explained on the hypothesis of "shock," lowered blood-pressure, damaging action of centripetal stimulation, etc. I do not think anyone would advance the theory that in two hours a large number of Purkinje cells could be absolutely removed. But the question arises, was the animal normal before the experiment? This can not be answered. The blood-pressure of P. 4 was 40 mm. to 60 mm.

In series 3 the following report can be made:—

P. 2 is the only material which need claim our attention. The Purkinje cells are in perfect condition. At the commencement of the experiment the blood-pressure was 150 mm.; at the end of the work it had fallen to 60 mm.

In series 4 and 5 a factor is introduced which we do not find in the other series. I refer to gross traumatizing of cerebral tissue. In each case there is noted: "Poor transfusion." Had we found extensive changes in the Purkinje cells it would have been hard to draw any conclusion. From the ten cases in series 1 and the one case in series 3 I would argue that any marked change in the Purkinje cells was more likely to be due to trauma practically in the immediate neighborhood. As a matter of fact there is little if any more change than is found in S. 155, S. 158 and P. 3.

CONCLUSIONS.

In drawing conclusions from this work we must bear in mind two points. The first is that the baneful effect of serious hemorrhage on the central nervous system has been well recognized for years. Hoche has shown[1] how rapidly the central nervous system is affected by hemorrhage and in the experimental work incident to a paper on "Hemorrhage into the Ventricles"[2] I found how

[1] *Neurol. Centralbl.*, 1895, No. 14, p. 754, and 1900, p. 994; also *Berliner klin. Wchnschr.*, 1900, No. 22, p. 479.

[2] *Journal of A. M. A.*, July 18, 1908.

quickly the cortex of the brain and the lateral columns of the cord lost their faradic excitability in severe hemorrhage. Let us remember this point in considering P. 4, P. 6, P. 7 and P. 8.

The second point to bear in mind is the severity of the stimuli in P. 2.

My conclusions are therefore as follows:

1. Lowered blood-pressure and peripheral trauma such as caused by surgical operations under anesthesia have no demonstrable effect on the Purkinje cells of the cerebellum.

2. The syndrome known as "shock" is totally unconnected with any demonstrable change in the Purkinje cells of the cerebellum.

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The influence of nocuous stimuli in the production of shock, and the failure of this influence to support the anoci theory of shock.

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The experiments reported in this communication have been performed for the purpose of investigating the influence of nocuous stimuli in the production of shock, by comparing with controls the shock-producing effect of severe and prolonged electrical stimulation to the peripheral sensory nerves in animals rendered susceptible to shock-producing influences by a reduction of their blood pressure.

Although an animal may be in severe shock with a high blood pressure, yet a fall of blood pressure always occurs before death and may be regarded as the most striking characteristic of shock. A diminution of blood pressure may, therefore, be legitimately considered to favor the development of shock, in other words, to render an animal a more sensitive test-subject upon which to investigate shock-producing influences. Such a method of experimentation would avoid the difficulty in estimating different degrees of shock in the experimental animals and would permit