The sections are cleared in xylol and mounted in turpentine balsam. The tigroid bodies and the chromatin of the nucleus and nucleolus stain of a dark blue color; while fibrillary and interfibrillary structures stain red. The method is very safe and reliable.

Harris's Method of Staining with Toluidin Blue.—The tissues are hardened in mercuric chloride, stained in carbolic-acid-water solution of toluidin blue for several minutes, differentiated in alcohol, cleared, and mounted in balsam. If desired, benzo-purpurin may be used as a contrast stain.

Method of Staining with Thionin.—Sections hardened in alcohol or sublimate or formalin are embedded in paraffin and fixed to the slide in the ordinary way. The staining is carried out with a concentrated aqueous solution of thionin, the dye being allowed to act for from three to five minutes. The sections are quickly washed in water and are then differentiated in a ten-per-cent. solution of aniline oil in absolute alcohol. They are cleared in oil of cajeput, then passed through xylol and mounted in xylol balsam.

Gram's Method of Staining, with Gentian Violet, Tissues Which have been Hardened in Alcohol.—Sections are cut in celloidin or paraffin. They are then stained in Ehrlich's solution of gentian violet, which consists of: gentian violet, 1; alcohol, 15; aniline oil, 3; water, 80. The sections are transferred, after staining, to a slide, spread out flat, and treated with the following solution: iodine, 1; iodide of potassium, 2; water, 300. They are then dehydrated in absolute alcohol, cleared in xylol, and mounted in xylol balsam.

Weigert's Fibrin Stain with Gentian Violet.—Sections from tissue hardened in alcohol are stained in Ehrlich's aniline gentian violet (*vide supra*). They are then placed on a slide and blotted with filter paper covered with Lugol's solution. After this has been allowed to act for from fifteen to thirty seconds the sections are blotted again. They are then dehydrated and cleared in a mixture of two parts of aniline oil with one part of xylol. This treatment is followed by pure xylol, in which the sections are washed until all the aniline oil has been removed. They are then mounted in xylol balsam. The method is of particular advantage in pathological histology.

Method of Staining with Aniline Blue Black.—Sections are stained for from thirty to sixty minutes in the following solution: aniline blue black, 0.25; distilled water, 100. The sections are then washed in water, dehydrated in alcohol, cleared in creosote, and mounted in balsam.

The Method of Staining with Saffranin.—Sections of tissue fixed in Flemming's solution are stained in a concentrated aqueous solution of saffranin for from twelve to twenty-four hours. They are then carefully differentiated in absolute alcohol, or, if necessary, in weak acid alcohol. The sections are cleared in oil of cloves and mounted in balsam. With proper differentiation karyokinetic figures are intensely stained, while resting nuclei retain only a feeble pink tint.

Rosin's Method of Staining with the Triple Stain of Biondi-Ehrlich.—Sections which have been hardened in alcohol and embedded in celloidin are treated as follows: They are stained for one minute in the following solution: one part of one-half-per-cent. solution of acid fuchsin is added to four parts of a solution of the following constitution: dry triple stain (Grübler), 0.4; distilled water, 100; 0.5 per cent. acid fuchsin solution, 7 (if the sections are not embedded in celloidin they can be stained for five minutes in the latter solution alone).

After staining, the sections are quickly washed in distilled water which is changed once, the washing requiring from one to two minutes; they are then treated for ten seconds with a feeble aqueous solution of acetic acid (one drop of glacial acetic acid in 100 c.c. of distilled water); they are then again washed in distilled water for sixty seconds to remove all trace of acetic acid. Differentiation is carried out with the aid of absolute alcohol for from two to three minutes, during which clouds of violet color are given off. The sections are cleared in xylol and mounted in balsam. The method requires considerable practice before good results are obtained.

C. Methods Which Demonstrate Especially the Myeline Sheaths.—*Method of Exner.*—Pieces of perfectly fresh tissue not more than 1 cm. broad and 0.5 cm. thick are placed in a one-per-cent. solution of osmic acid. There must be at least ten times as much osmic-acid solution as there is tissue by volume. After two days the osmic acid is changed. The tissue can be examined between the fifth and the ninth day. It is washed in water, dried on the surface with filter paper, fastened to cork by means of sealing wax, and then sectioned in the microtome. The sections are placed in glycerin, whence they are brought upon a glass slide and treated with a drop of weak solution of ammonia (20 drops of liquor ammonii caustici in 50 c.c. of water). The myeline sheaths of the nerve fibres are stained black; all other structures remain pale.

Weigert's Method of Staining Myeline Sheaths.—Tissues are hardened in Müller's fluid or in formol followed by Müller's fluid, or in Orth's fluid or in formol followed by four days in the following solution: Potassium bichromate, 5 parts; chrome alum, 2 parts; dilute water, 100 parts. The blocks of tissue are transferred without washing into alcohol and are embedded in celloidin. The sections are placed for twenty-four hours in a saturated solution of acetate of copper diluted with an equal volume of water. They are stained for from twenty minutes to twenty-four hours in the following solution: hæmatoxylin, 1; absolute alcohol, 10; lithium carbonate, 1; distilled water to make up 100 parts. The sections are next washed in water and differentiated in the following solution: borax, 2; ferricyanide of potash, 2.5; distilled water, 100. The sections are then thoroughly washed in water, dehydrated in alcohol, cleared in xylol or carbol xylol, and mounted in balsam. The myeline sheaths of medullated nerve fibres are stained bluish black, the background being of a brownish-yellow color.

Weigert's Rapid Myeline Stain.—Small blocks of tissue are placed for from four to five days in ten-per-cent. solution of formol (four-per-cent. solution of formaldehyde); after this they are placed in a mordant of the following formula: bichromate of potash, 5 parts; chrome alum, 2 parts; boiling water, 100 parts. If desired the hardening and mordanting can be done together by adding 10 gm. of the ten-per-cent. solution of formol to 100 parts of the mordant. If desired, instead of the above treatment Weigert's copper mordant (used for his neuroglia stain) may be employed. This consists of five-per-cent. copper acetate, five-per-cent. acetic acid, and two-and-one-half-per-cent. chrome alum dissolved in water. It has the advantage of making no precipitates on the tissues, and, further, does away with the necessity of treating the sections with copper acetate after they have been cut. If left longer than eight days in the fluid the tissues become very brittle.

Pal's Modification of Weigert's Stain for Myeline Sheaths.—The tissues are prepared as for Weigert's method, except that the sections are not treated with acetate of copper. Sections are stained in Weigert's hæmatoxylin solution for from twenty-four to forty-eight hours in the cold; they are then washed in lithiated water (four per cent.); after washing they are placed in a freshly prepared 0.33-per-cent. solution of potassium permanganate for from twenty to thirty seconds, or until the gray matter looks yellowish. The sections are transferred immediately to the following solution: oxalic acid, 1; potassium sulphite, 1; distilled water, 200. The differentiation is watched closely to see that it does not go too far. Should it not proceed rapidly enough the sections are put back into the solution of potassium permanganate and again exposed to the oxalic-acid solution. When the differentiation has gone far enough the sections are washed out in water, and transferred to a strong solution of lithium for five or ten minutes until they turn of an intense blue color. They are finally thoroughly washed in water, dehydrated in alcohol, cleared in xylol or carbol xylol, and mounted in balsam.

Schaefer's Modification of Weigert's Method.—The treatment is the same as for Weigert's method, except that the sections after having been passed through water are left in Marchi's fluid for some hours; they are then thoroughly washed and stained in the following solution: hæmatoxylin, 1; absolute alcohol, 10; two-per-cent. solution of acetic acid, 100. After they have remained in this fluid for twenty-four hours the sections are washed in water and decolorized according to Pal's method (*vide supra*).

Vassale's Modification of Weigert's Method.—Sections are prepared as in the method of Weigert. They are then stained in a one-per-cent. aqueous solution of hæmatoxylin for from three to five minutes, after which they are washed in water, exposed for a few minutes to the action of a saturated solution of neutral acetate of copper. They are then washed in water and differentiated by Weigert's ferricyanide solution. They are again washed in water, dehydrated in alcohol, cleared in carbol xylol, and mounted in balsam.

Berkley's Modification of Weigert's Stain.—Pieces of tissue 2 mm. in thickness are hardened in Flemming's solution for from twenty-four to thirty hours. They are transferred directly to absolute alcohol which is changed twice on the following day. As soon as the consistency will permit of the making of very thin sections the pieces of tissue are embedded in celloidin and cut under ninety-five per cent. alcohol. After quick washing in water they are laid in a saturated solution of acetate of copper and heated on a water bath for from twenty to thirty minutes, at a temperature of from 100° to 110° F. The fluid is allowed to cool, after which the sections are quickly washed in water and then stained in the following fluid freshly prepared: to 50 c.c. of boiled distilled water are added 2 c.c. of saturated solution of lithium carbonate. The boiling is continued for another minute, after which 1.5 or 2 c.c. of a ten-per-cent. solution of hæmatoxylin in absolute alcohol is added little by little with constant stirring. As soon as cool the fluid is ready for use. Sections placed in the stain are warmed on a water bath to a temperature of 100° F. for from fifteen to twenty minutes or longer. After cooling they are twice washed in water, then differentiated in Weigert's borax ferricyanide solution diluted with one-half or one-third its volume of water. Usually five or six minutes suffice to complete the decolorization. The sections are washed in two waters, dehydrated in alcohol, cleared in oil of bergamot, and mounted in balsam.

Herrick's Modifications of Weigert's Stain for Comparative Work.—For the formulæ used by Herrick his original article is referred to ("Report upon a Series of Experiments with the Weigert's Methods—with Special Reference for Use in Lower Brain Morphology." The State Hospitals' Bulletin, Utica, vol. ii., 1897, pp. 431–461).

Marchi's Method of Staining Degenerated Myeline Sheaths.—Small pieces of tissue are hardened for eight days in Müller's fluid, transferred without washing to Marchi's fluid, which consists of two parts Müller's fluid mixed with one part of a one-per-cent. solution of osmic acid. In the latter fluid the bits of tissue remain for from five to ten days, after which they are washed for twenty-four hours in running water, hardened in alcohol, embedded in celloidin, and cut in the microtome. The sections are cleared in xylol and mounted in xylol balsam. Chloroform balsam is to be avoided. Degenerated myeline sheaths stain of an intense black, while all others remain of a light yellow color or of a slightly grayish tint. The method demonstrates of course only myeline sheaths in the process of degeneration. If degeneration has existed for over three months and the myelin has been absorbed the degenerated fibres are not demonstrable by Marchi's method. The method has proved to be of especial value in experimental work. It is also of great value in studying recent degenerations in human cases in which fresh autopsies can be obtained.

The tissues may be fixed, if desired, in formol before treatment with Marchi's fluid, but the results are not quite so satisfactory as when the original procedure is employed. Formol tissues have the advantage that they warp less than those prepared by the original method.

Vassale's Modification of Marchi's Method.—Instead of two parts of Müller's fluid to one part of the one-per-cent. osmic-acid solution, Vassale uses three parts, and, further, to 100 c.c. of the Marchi fluid thus prepared he adds twenty drops of pure nitric acid. He asserts that by this method precipitates are less abundant and the degenerated fibres stand out much more sharply from the other tissues.

Hamilton's Modification of Marchi's Method.—According to this method Marchi's fluid is applied after the sections are made. The sections are placed in a fluid obtained by macerating brains hardened in bichromate, in chromic-acid solution, and filtering. This bath, he asserts, renders the sections susceptible to the osmium reaction when they are afterward treated with Marchi's fluid. The method requires further testing. The writer's experience with it has not been satisfactory.

D. Methods for the Especial Demonstration of Axones or Axis-Cylinder Processes.—Golgi's method and the method of vital staining of Ehrlich are the best we have for the demonstration of the external form of axones. For the examination of the finer internal structure of axones, various methods have been recommended.

Van Gieson's Method.—Tissues hardened in Müller's fluid are sectioned after embedding in celloidin. The sections are stained for from three to five minutes in Delafield's hæmatoxylin, thoroughly washed in water, and afterward stained in a mixture of saturated picric-acid solution with saturated solution of acid fuchsin. They are then washed quickly in water, dehydrated in alcohol, cleared in oil of origanum, and mounted in balsam. The axis cylinders stain deep red in the acid fuchsin, the myeline sheaths take a yellow tint from the picric acid; all nuclei stain in hæmatoxylin, while neuroglia tissue takes the acid fuchsin, especially in sclerotic areas.

Stroebe's Method for Axis Cylinders.—Tissues hardened in Müller's fluid are sectioned after embedding in celloidin. The sections are stained in a saturated aqueous solution of aniline blue until they are of a deep blue-back color. The staining requires from fifteen to sixty minutes. The sections are then washed in water, differentiated in absolute alcohol to which has been added a few drops of a one-per-cent. solution of caustic potash dissolved in absolute alcohol and filtered after standing twenty-four hours. The sections remain in this fluid until they are of a light brownish-red color, which usually appears after a very few minutes. They are then washed in water, in which the sections turn light blue. As a contrast stain a dilute solution of saffranin is allowed to act for from fifteen to thirty minutes. Sections are dehydrated in absolute alcohol, cleared in xylol, and mounted in balsam. Axones stain deep blue, myeline sheaths orange red, glia fibres blue. The method requires some practice before good results can be obtained.

Held's Method for Studying Axones.—No better mode perhaps of studying the finer internal structure of axones has been devised than Held's modification of Nissl's methylene-blue staining (*vide supra*). The sections must be very thin. The neurosomes and fibrillary or honeycomb structures are exquisitely brought out by this procedure. For showing the neurosomes alone in all parts of the neurones, perhaps the best method is another introduced by Held. The tissues are fixed in a solution of neutral chromate of potash, sectioned in paraffin, and stained with iron hæmatoxylin.

E. Methods Especially Applicable to Neuroglia.—*Weigert's Neuroglia Stain.*—This stain, the method for which was published in 1895 by Carl Weigert of Frankfort, is carried out as follows: Tissues are fixed and mordanted for eight days in the following solution: acetate of copper, 5; acetic acid, 5; chrome alum, 2.5; formol, 10; distilled water, 100. The chrome alum must be dissolved in boiling water, while the acetate of copper and acetic acid are added afterward. If these directions are not followed a precipitate will be formed.

In particular, Weigert advises boiling the chrome alum and water in an enamelled saucepan; when the boiling is active after the chrome alum has been dissolved the flame is turned out and the acetic acid and finely powdered neutral acetate of copper are added. One stirs vigorously until one can feel with the glass rod that the copper salt has almost entirely dissolved. The fluid is then allowed to cool and will remain clear. Tissues which have been hardened for four days in formalin can be placed in this fluid and left for four or five days at the temperature of the thermostat or for eight days at the room temperature. It is perhaps better, however, to harden directly in a fluid to which ten-per-cent. formol has been added. The fluid should be changed on the second day. Weigert states that tissues never become brittle in this fluid. When desired to make sections the pieces of tissue are washed with water, dehydrated in alcohol, and embedded in celloidin. The sections are next placed in some reducing fluid. Weigert recommends a mixture of five-per-cent. chromogen and five-per-cent. formic acid (specific gravity, 1.20) in water. This mixture is filtered carefully, and before it is used one adds to 90 c.c. of the fluid 10 c.c. of a ten-per-cent. solution of ordinary sodium sulphite (that used in photography). The sections are placed first for ten minutes in a 0.33-per-cent. solution of permanganate of potash. They are then washed in water, after which the water is removed and the reducing fluid above mentioned is poured upon the sections. After a few minutes the sections which were turned brown by the permanganate of potash become decolorized. Weigert recommends that the sections be left for from two to four hours in the chromogen mixture.

After removal from the reducing fluid and washing twice in water the sections are placed in a simple saturated aqueous solution of chromogen (made by dissolving five parts of chromogen in one hundred parts of distilled water and filtering).

The sections remain in this solution over night. The longer they stay in this fluid the more stained are the nervous elements of the tissue. They are washed twice in water, after which the sections are ready for the stain. If they cannot be stained at once the sections should be preserved in the following mixture: eighty-per-cent. alcohol, 90 c.c.; five-per-cent. solution of oxalic acid, 10 c.c.

The sections are stained in a methyl-violet solution prepared in the following way: methyl violet in excess is added to hot seventy-per-cent. alcohol, and after cooling the fluid is poured off from the undissolved methyl violet. To every 100 c.c. of this solution are added 5 c.c. of a five-per-cent. aqueous solution of oxalic acid. The sections are placed upon a glass slide, treated with a solution of iodine and iodide of potash (as in Weigert's fibrin stain), after which they are differentiated in a mixture of equal parts by volume of aniline oil and xylol. They are then washed in xylol very carefully several times. Otherwise the preparations do not keep well. They are then mounted in balsam, exposed for from two to five days to diffuse daylight, and afterward kept in cabinets in the ordinary way.

An excellent staining method for neuroglia is that introduced by F. B. Mallory,* of Boston. The tissues are fixed in equal parts of a saturated aqueous solution of picric acid and a five-per-cent. solution of formalin. They remain in this for from four to seven days. The tissues are then transferred to a two-per-cent. solution of ammonium bichromate, where they remain for from one to two weeks. They are then washed in water, dehydrated in alcohol, and embedded in celloidin. The celloidin is removed from the sections, which are then stained feebly in carmine and afterward stained by Weigert's fibrin stain.

F. Methods for Demonstrating Fibrillar and Reticular Structures in the Nervous System.—S. Apáthy, of Klausenburg, has introduced several methods which are of the greatest value for staining the neurofibrils in lower animals. They do not stain, however, the same fibrils in vertebrates. Three principal methods have been introduced by Apáthy.

(1) *Staining of Fresh Tissue with Methylene Blue.*—This method is described in the *Zeitschr. f. wissensch. Mikr.*, Bd. ix., 1892.

(2) *Staining of Hardened Tissue with a Solution of Hæmatëin.*—The tissues may be fixed by any one of several methods: sublimate, sublimate alcohol, corrosive acetic, picric acid, Zenker's fluid, etc. After fixation the tissues may be kept in ninety-per-cent. alcohol until it is desired to stain them. The pieces should not exceed 5 mm. in thickness. They are stained in bulk in a solution of hæmatëin, prepared by successively pouring together equal volumes of the three following ingredients: one per-cent. hæmatëin tincture, concentrated glycerin, and nine-per-cent. alum solution with addition of salicylic acid and acetic acid. The hæmatëin solution is prepared from hæmatoxylin by ripening it. A one-per-cent. solution of hæmatoxylin crystals in a seventy-per-cent. solution of pure alcohol is first made. This is allowed to stand in a flask of good glass which is not quite full. The oxidation of the hæmatoxylin to hæmatëin should go on at the room temperature for from six to eight weeks. The alum solution is prepared as follows: 9 parts of alum, 3 parts of glacial acetic acid, and 0.1 part of salicylic acid are dissolved in 100 parts of water.

The tissue remains in the dye for at least forty-eight hours. It is then washed for twenty-four hours in pure double distilled water, which must be often changed. The tissue is then placed in feebly alkaline water for from three to five hours, after which it is returned for two hours (at most) to distilled water. It is then quickly dehydrated in alcohol and embedded in either celloidin or paraffin.

(3) *Staining of Fresh and Fixed Tissues by the Gold Method.*—The tissue is cut into thin pieces and placed in a solution of yellow gold chloride. The amount of fluid should be ten times the volume of the object. After the treatment with the gold solution the tissue is exposed to the light in a one-per-cent. solution of formic acid (crystallized, specific gravity, 1.223) in distilled water. The tissue should be exposed to direct or indirect sunlight from all sides, the vessel containing it sitting upon a mirror. The exposure to light should not be too short, but exposure for more than twenty-four hours is not advisable. At least six or eight hours is always needed. For full particulars regarding the methods, Apáthy's* article is referred to.

Bethe has recently introduced a method by which the neurofibrils in the tissues of human beings and other mammals can be stained; it is as follows: Fresh tissue in discs 4 to 10 mm. thick are laid upon filter paper and immersed in nitric acid of a strength of from three to seven and one-half per cent., where they remain for twenty-four hours, the pieces being frequently turned. They are then transferred to ninety-six-per-cent. alcohol, where they remain for from twelve to twenty-four hours. The pieces are then immersed for from twelve to twenty-four hours in the following mixture: ammonia (specific gravity, 0.95 to 0.96), 1 part; water, 3 parts; ninety-six-per-cent. alcohol, 8 parts. The temperature should not exceed 20° C. The pieces are then transferred for from six to twelve hours to ordinary alcohol. After this they are placed in acid alcohol of the following constitution: hydrochloric acid, concentrated, 1 part; water, 3 parts; ninety-six-per-cent. alcohol, 8–12 parts. In this the tissues become light yellow or nearly white if they have only been feebly acted upon by the nitric acid. After treatment with acid alcohol the tissues are again placed in ordinary alcohol for from ten to twenty-four hours. They are then washed in water for from two to six hours. After this they are molybdanized. The blocks of tissue are transferred to a four-per-cent. solution of ammonium molybdate, where they remain for twenty-four hours. They are then quickly washed in distilled water, dehydrated in ninety-six-per-cent. alcohol for from ten to twenty-four hours, then in absolute alcohol for the same length of time; cleared in xylol or toluol and embedded in paraffin (not in celloidin).

The neurofibrils and the Golgi network can be stained by this method.

For further details and for a modification of the method, Bethe's original article is referred to.*

* Mallory, F. B.: Ueber gewisse eigenthümliche Färbereactionen der Neuroglia. Centralbl. f. allg. Pathol. u. path. Anat., Jena, Bd. vi., 1895, October 31st, S. 753–758.

* Apáthy, S.: Das leitende Element des Nervensystems und seine topographischen Beziehungen zu den Zellen. I. Mittheilung, Mittheil. d. Zool. Station Neapel, Bd. xii., p. 495–748.

* Bethe, A.: Das Molybdanverfahren zur Darstellung der Neurofibrillen und Golginetze im Centralnervensystem. Zeitschr. f. wissensch. Mikr., Bd. xvii., 1900, S. 13–35.

Microscopic Appearances.

The brains of different animals vary, of course, in size and complexity. The present article deals almost entirely with the minute anatomy of the human brain.

In human beings we designate as brain or encephalon that portion of the central nervous system enclosed within the skull. It is continuous at the level of the great occipital foramen with the spinal cord or medulla spinalis. The brain, like the spinal cord, is enclosed in membranes known as meninges: (1) A firm tough membrane (dura mater encephali); (2) a very delicate membrane closely crowded with minute blood-vessels and closely attached to the surface of the brain substance (pia mater encephali); and (3) a membrane between the two former membranes, (arachnoidea encephali).

The gross anatomy of the brain is described in another article in this Handbook.

With the naked eye it is seen that the main mass of the brain consists of a very white substance, the so-called white matter, or *substantia alba*, and a gray substance, the so-called gray matter, or *substantia grisea*. The substantia alba is more abundant than the substantia grisea. In general it may be said that in the brain the gray substance is chiefly on the surface of the organ and in certain large gray masses, the so called basal ganglia: while the white matter is situated internally, being surrounded by the gray. The relative positions of white and gray matter are, in the brain, exactly the reverse of those in the spinal cord, where the gray matter is inside and the white matter outside. In the region of the brain nearest to the spinal cord, a very irregular arrangement of gray and white matter is met with, the various masses of gray matter being known as "nuclei" of the gray substance. These nuclei include among other structures the nuclei of origin and termination of various cerebral nerves.

Histological research has shown that the nervous system, like the other tissues of the body, consists of an aggregation of cells and intercellular substances derived from cells. All the cells of the central nervous system except those of the meninges and the blood-vessels, with the tissue immediately adjacent to the latter, are believed to be derived from the ectoderm or outermost layer of the embryo.

The cells in the brain may be divided into two main groups: (1) the true nerve cells or *neurones*, and (2) all other cells including those of the *neuroglia* and *ependyma*.

The *nerve cells*, or *neurones*, differ markedly from other cells in the body in that portions of the protoplasm are drawn out in many instances to form threads of great length. Nowhere in the body do cell processes so long, so complex, so much branched, and so delicate occur as in the nervous system. While nerve cells vary distinctly in size, shape, and mode of branching, the most common type possesses the following characteristics: each nerve cell or neurone consists of a *cell body* or *perikaryon*, a number of protoplasmic processes or *dendrites*, and a single long, delicate process which often becomes surrounded with an especial fatty sheath (myelin), the so-called *axone* or axis-cylinder process.

The nerve cells, compared with other cells of the body, are as a rule, large, contain large nuclei, poor in chromatin, and usually provided with a large nucleolus.

The *dendrites* or protoplasmic processes are thick at their origin and gradually diminish in calibre as they pass from the cell, owing to manifold subdivision. Through the multiplication of these processes the area of the surface of the protoplasm of the cell is enormously increased.

The *axone* differs from the dendrite in that it arises by a thin wedge of origin, usually from the cell body, but

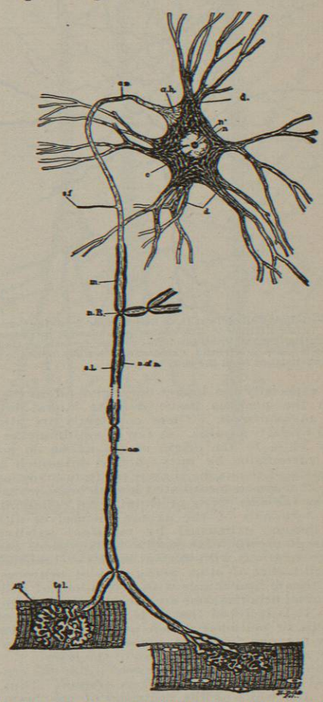

Fig. 905.—Schematic Representation of a Lower Motor Neurone. The motor cell from the ventral horn of the spinal cord, together with all its protoplasmic processes and their divisions, its axis-cylinder process with its divisions, side fibrils, or collaterals, and end ramifications (telodendrions or motor end-plates) in the muscle, represent parts of a single cell or *neurone*. *a.h*, Axone hillock devoid of Nissl bodies, and showing a tendency to fibrillation; *a.x*, axis cylinder or axone, also indistinctly fibrillated. This process, at a short distance from the cell body, becomes surrounded by a myeline sheath, *m*, and a cellular sheath, the neurilemma, the latter not being an integral part of the neurone; *c*, cytoplasm showing the dark-colored Nissl bodies and lighter ground substance; *d*, protoplasmic processes (dendrites) containing Nissl bodies; *n*, nucleus; *n'*, nucleolus; *n.R*, node of Ranvier; *sf*, side fibril; *n of n*, nucleus of neurilemma sheath; *tel*., motor end-plate or telodendrion; *m'*, striped muscle fibre; *s.L*., segmentation of Lantermann. (From "The Nervous System and Its Constituent Neurones," D. Appleton & Co., New York, 1899.)

sometimes from one of the dendrites near the origin of the latter. The axone has a smooth, regular surface and very even calibre, even when followed for a long distance from the cell body which gives it origin. The length of the axone may vary greatly. If it is very long it usually

becomes surrounded by a myeline sheath (*inaxone*, Golgi's cell type I.) (Fig. 905); if it is very short, terminating near the cell body, it does not become surrounded by a myeline sheath (*dendraxone*, Golgi's cell-type II.) (Fig. 906). Many

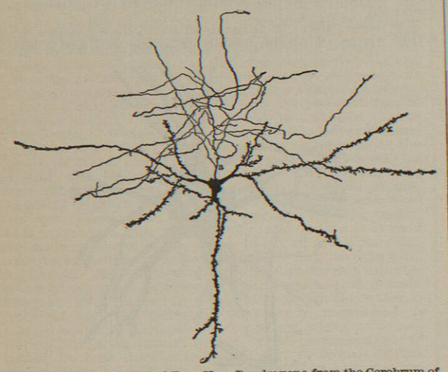

FIG. 906.—Golgi's Cell of Type II. or Dendraxone from the Cerebrum of a Cat. (After Kölliker.) The coarse protoplasmic processes, *x*, are easily distinguishable from the axis-cylinder process, *a*, though the latter soon loses its identity, exhausting itself by multiple division at a short distance from the cell.

axones, especially the longer ones, give off as they pass through the nervous tissue delicate lateral branches known as *collaterals*. These collaterals are also surrounded by fatty sheaths. A few lateral branches given off very close to the origin of the axone do not become surrounded by fatty sheaths inasmuch as this portion of the axone is also free from investing sheath. These non-medullated lateral branches are known as the *side fibrils* of Golgi. All collaterals and the terminals of the axones themselves ultimately become exhausted by manifold subdivision in regions where these fine subdivisions can enter into relations with the cell bodies or branches of the cell bodies of other nerve cells or neurones. These ultimate branchings with formations of delicate terminal arborizations are the so-called *telodendrions*. It is believed that it is the great mass of nerve cells or neurones which are responsible for the truly nervous functions, namely, the reflex, instinctive, and volitional activities of the body.

The *ependymal cells* are those which line the central canal of the central nervous system. Thus, they line the walls of the ventricles of the brain, those of the aqueduct of the cerebrum and the central canal of the spinal cord.

The *neuroglia cells*, also ectodermal in origin, are widely distributed throughout the nervous tissues of the brain and are believed by most observers to represent supporting cells. They include the spider cells, the stellate glia cells, and various other forms of cells. They are present in both the white and the gray substance.

The *intercellular substances* in the brain have only begun to be worked out; while many believe that the only intercellular substances present are the fluids of the lymph derived from the blood, others maintain the existence of an enormous number of fibrils between the cells. Studies of Weigert indicate the existence of neuroglia fibrils differentiated from the neuroglia cells. Many of these fibrils pass directly through the bodies of the glia cells. The studies of Apáthy and Bethe indicate the presence of highly differentiated fibrils inside the bodies of the true nerve cells or neurones. These fibrils they believe pass from one neurone to another. Nissl has gone even further and asserts that great masses of these fibrils exist outside the cells, and he believes that the peculiar character of the gray matter, especially of that of the cerebral cortex, is due to the presence of these fibrils between the cells. The views of Nissl have not as yet been confirmed.

The gray and white matter of the brain are richly supplied with blood by means of a very indirect network of capillaries derived from the intracranial blood-vessels. The supply of blood to the gray substance is much more copious than that to the white substance.

After these preliminary statements the cells and intercellular substances of which the brain is composed may be considered more in detail.

The *nerve cells* or *neurones* will be considered first. A striking feature is the uniformity in type met with in various parts of the brain. There are, however, differences even in external form which are easily recognizable by the trained histologist. The cells in certain of the gray masses have so distinct a type that their origin can be predicted at once when they are seen under the microscope. The differential features lie in the form and size of the cell body, the characters of the dendrites and axones, and the relations of these to the cell body.

Among the *cell bodies* or *perikaryons* there are great variations in size. Thus, for instance, the large cells of Betz in the paracentral lobule possess cell bodies many times the size of the minute perikaryons of the olfactory granules. The shape, too, of the cell bodies varies much. The pyramidal cell of the cortex of the cerebrum, the flask-shaped cell of Purkinje in the cerebellar cortex, and the large multipolar ganglion cells of Deiters' nucleus may be recalled.

The *dendrites* of the nerve cells are usually numerous, rarely single. These processes appear to be much drawn-out portions of the cell body. The relation of the processes to the cell body varies with different types of neurones. Thus, in the nuclei of origin of the motor

FIG. 907.—Photomicrograph of a Normal Purkinje Cell from the Human Cerebellar Cortex. (After Berkley.)

cerebral nerves, large dendrites project from nearly all portions of the surface of the cell body. From the cells in the hippocampus, dendrites project only from the two poles of the cell. In the cerebellar cortex the neck of the flask-shaped cell is a huge dendrite which subdivides

soon into two or more large branches, which then go on to subdivide over and over again until a forest of dendritic branches has been formed which has no equal elsewhere in the nervous system (Fig. 907). In the cerebral cortex the pyramidal cells give off dendrites from the apex and from the lateral angles of the pyramid (Fig. 908). While in some of the neurones the various dendrites are approximately equal in size and in extent of distribution (cells of motor nuclei), in other neurones the size and mode of distribution of fibres from a given cell may be very different. Thus, taking a pyramidal cell of the cerebral cortex again for an example, while the apical dendrite forms a large, strong, straight branch which as a rule extends a long distance from the cell before breaking up into an end tuft of subdivisions, the smaller dendrites given off from the angles of the pyramid are of much smaller calibre, are often tortuous, branch quickly after leaving the cell body, and soon exhaust themselves by multiple subdivision in an area close to the perikaryon. The branches of the individual dendrites, no matter how far away from the cell they terminate, appear to end free. It was believed that they always came into direct

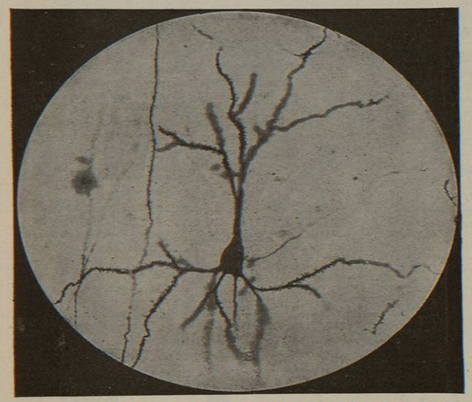

FIG. 908.—Photomicrograph of a Normal Pyramidal Cell from the Cerebral Cortex of the Guinea-Pig. (After Berkley.) The single-branched apical dendrite and the basal dendrites show distinctly the lateral buds o, "gemmules." The axone is relatively smooth.

contact or even into more intimate connection with the walls of blood-vessels, but this view has been given up. It has been proven, however, that they come into intimate relation with the terminals of the axones and collaterals of other neurones, and it is believed by many that this relation is one which subserves the purpose of a transference of impulses, that is to say, the relation is thought to be a conduction relation. The surface of the dendrites is by no means smooth, and in this particular is in strong contrast with the surface of the axones. In well-impregnated Golgi preparations and in certain methylene blue preparations it is possible to make out minute projections from the surface of certain of the dendrites, especially from the apical dendrites of the pyramidal cells in the cerebral cortex. These prickle-like projections, when seen under very high powers, have a nodular extremity. They are the so-called lateral buds or gemmules (Fig. 909). In the course of a dendrite definite bulgings are sometimes met with. These bulgings or varicosities are at times found in what are believed to be normal tissues, but appear to be more frequent in the brains of individuals dead of certain pathological processes. In normal individuals these varicosities or bulgings are probably to be regarded as artefacts (Fig.

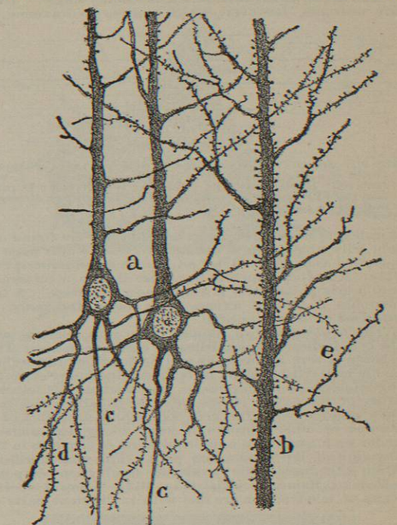

FIG. 909.—The Lateral Buds or Gemmules on the Apical Dendrites of the Pyramidal Cells of the Cerebral Cortex. Methylene-blue preparation. (After Ramón y Cajal, S., "Textura del sistema nerviosa," p. 55, Fig. 13.)

910). Their pathological significance in abnormal brains is difficult to determine. A few nerve cells

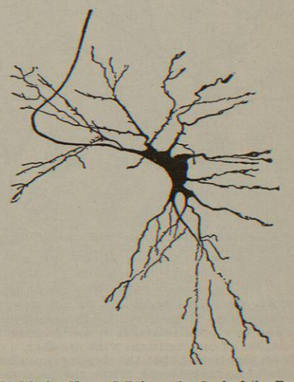

FIG. 910.—Multipolar Nerve Cell from the Cord of the Embryo Calf, Showing Varicosities of the Dendrites. (After Van Gehuchten.)

have been described in which no dendritic processes could be made out. They are the so-called adendritic neurones.

The *axone*, as has been stated, is usually single. There are neurones, however, which possess two axones, the

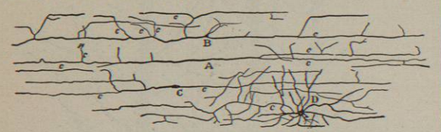

FIG. 911.—Special Cells (Polyaxones) of Molecular Layer of Cerebral Cortex of a Dog One Day Old. (After Ramón y Cajal.) *A*, Fusiform cell; *B*, triangular cell; *C*, another fusiform cell; *D*, polygonal cell with numerous dendrites and an axone which divides repeatedly; *c*, axones.

so-called *diaxones*. In the cerebral cortex are found certain cells which possess several processes which must be regarded as axones. They are known as *polyaxones* (Fig. 911). An axone which in its course divides or bifurcates into nearly equal parts is known as a *schizaxone*. A few neurones devoid of axones have been designated as *anaxones* or *amacrine cells*.

The *telodendrions* of axones come into relation with the cell bodies and dendrites of other neurones. This relation is very intimate, as will be described farther on, and is believed by many to be a conduction relation for the transference of impulses. Inasmuch as the telodendrion of the axone of one neurone usually comes into such relation with the cell bodies and dendrites of a number of other neurones, it seems likely that there is under such conditions a multiplication of elements in the direction of the conducting path. This anatomical relation is the basis of the "avalanche conduction" hypothesized by Ramón y Cajal (Fig. 912). Certain special forms of telodendrion are met with in different parts of

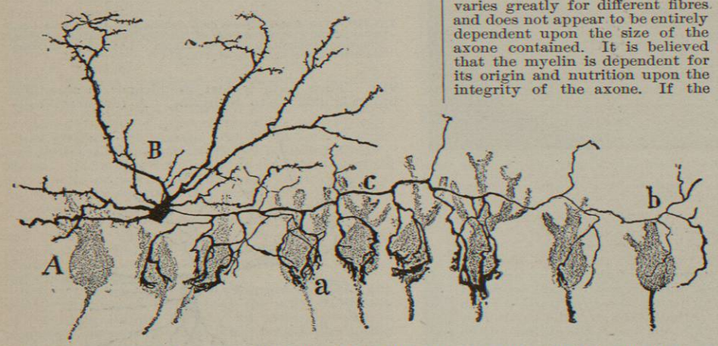

FIG. 912.—The neurone B has an axone which gives off a number of branches; by means of these branches conduction-relation with the cell bodies of a number of Purkinje cells is established. (After Ramón y Cajal, S., "Textura del sistema nervioso," Madrid, 1889, p. 69, Fig. 19.)

the brain. Of these the calyx-like terminals in the nucleus of the trapezoid body and the climbing fibres of the cerebellar cortex (Fig. 913) may be mentioned. The term *synapsis* has been introduced to designate the anatomical relation of one neurone with another.

It has been mentioned that the dendraxones have short axones without an investment, while the inaxones possess long axones provided with a myeline sheath. In the central nervous system these long axones do not, however, possess any sheath which corresponds to the neurilemma of the peripheral nerves.

The *myeline sheath* of the axones is strongly refractive and glistening. Examined fresh it is quite homogeneous, but soon undergoes certain alterations. One of the most marked of these is the appearance of certain oblique splits in the medullary substances which divide the myelin into a number of segments, known as Lantermann's segments. Treatment of the myeline sheath with hot ether or alcohol dissolves out a large portion of the myelin, but leaves behind a delicate network which is very resistant (Fig. 914). This network is not digestible in artificial pancreatic juice. It is the so-called neurokeratin of Ewald and Kühne, and is believed to be allied chemically to the keratin of the epidermis.

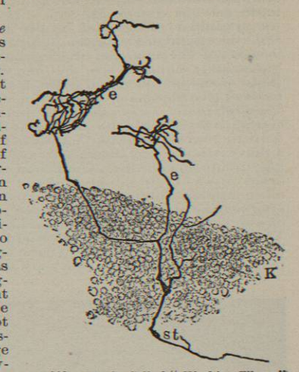

FIG. 913.—The So-Called "Climbing Fibres" of the Cerebellar Cortex from the Brain of a Child a Month and a Half Old. (After Kölliker.)

The myeline sheath at certain intervals shows definite indentations, the nodes of Ranvier. The thickness of the myeline sheath varies greatly for different fibres and does not appear to be entirely dependent upon the size of the axone contained. It is believed that the myelin is dependent for its origin and nutrition upon the integrity of the axone. If the axone be cut through, the myeline sheath as well as the axone distal from the point of section undergoes complete degeneration and is absorbed usually in about three months.

FIG. 914.—Nerve Fibre After Treatment with Ether. (After Ramón y Cajal, S., "Textura del sistema nervioso," Madrid, 1899, p. 200, Fig. 62.)

The medullated collaterals possess the same structure and undergo the same mode of temination as do fine axones. The non-medullated side fibrils behave like the non-medullated axones of dendraxones. Some of the non-medullated side fibrils, however, have the peculiarity of running back to end in the form of flat terminal plates upon the cell body of the neurone to which they belong.

The axone close to the nerve cell is usually entirely devoid of any covering of myelin (Fig. 915). A reticular investment, however, has been demonstrated upon the cell bodies and dendrites by Golgi (Fig. 916). This in-

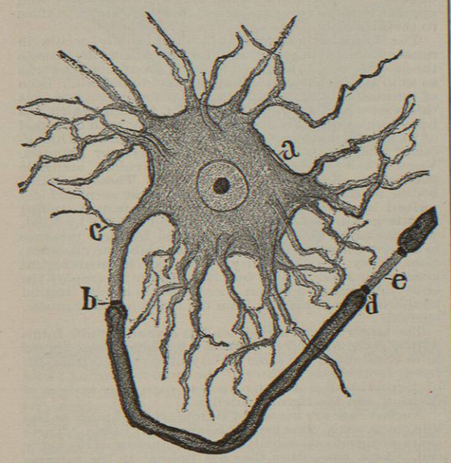

FIG. 915.—Methylene-Blue Preparation. The axone close to the perikaryon s devoid of myeline sheath. (After Ramón y Cajal, "Textura del sistema nervioso," Madrid, 1899, p. 113, Fig. 34.)

vestment may be homogeneous upon the finer branches of the dendrites. Its exact nature has not yet been determined, but Golgi suggests that it may be of the nature

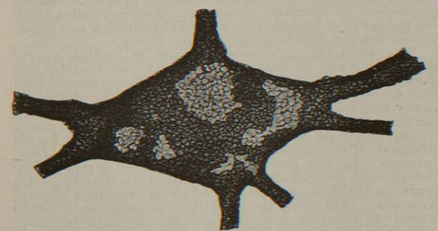

FIG. 916.—Nerve Cell Showing Reticular Investment. (After C. Golgi, *Arch. Ital. de Biol.*, Turin, t. xxx., 1898, p. 62.) The cell is from the ventral horn of the spinal cord of a cat.

of neurokeratin. These fine networks are drawn, as it were, like stockings over the perikaryon and dendrites. Golgi's network does not seem to be identical with the networks of Held and Bethe. Held's networks (Fig. 917) are believed to be formed by the subdivisions of fine terminal axones. The nature of Bethe's pericellular network (Fig. 918) is not yet clear.

We may pass now to a consideration of the finer structure of the protoplasm and nucleus of the nerve cell or neurone, the observations which have preceded having

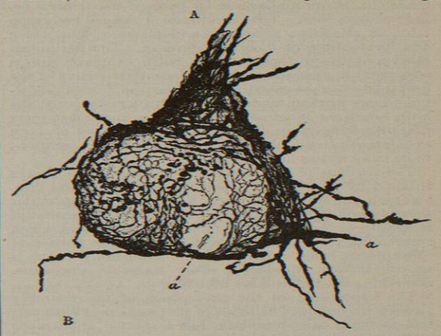

FIG. 917.—Pericellular Networks Believed by Held to be Formed by the Terminals of Axones. Golgi preparations from a cat twenty days old. Sections 70 μ thick. (After H. Held, *Arch. f. Anat. u. Physiol.*, Leipsic, 1897, Anat. Abth., Suppl. Bd., Taf. xiv., Figs. 5, 7, and 8.) A, Cell with network from nucleus nervi cochleæ ventralis. The pericellular network surrounds the whole cell and a dendrite passing upward. The fibre *a* corresponds to one of the thickened fibres of the n. cochleæ described by Ramón y Cajal and Held. Beyond the thickened spot fibrils go to join the general pericellular network.

dealt almost entirely with the external form of the neurone and its various branches. The protoplasm of the cell body and dendrites of the neurone varies consider-

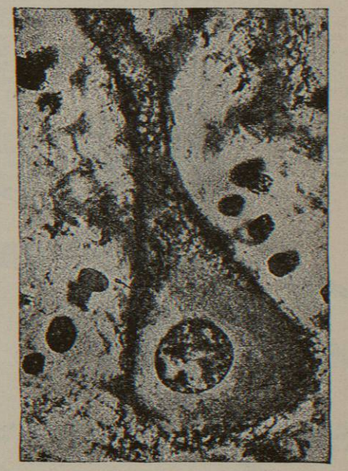

FIG. 918.—Network About Perikaryon and Dendrites Demonstrable by the Method of Bethe. (After F. Nissl, *München. med. Wochenschr.*, Bd. xlv., 1898, S. 1024, Figs. 1, 2.) Nerve cell from the nucleus dentatus of a dog.