nerve irritability is increased and the size of negative variation is increased. The same result is obtained if the nerve is tetanized; so Waller concludes that carbonic anhydride is produced during tetanization. As many other factors affect the negative variation in the same way, we cannot conclude from this observation that the conduction of the nerve impulse is accompanied by a metabolic change, leading to carbonic-anhydride formation.

The Action of Anæsthetics.—The anæsthetics, chloroform, ether, carbon dioxide, and alcohol all temporarily annihilate nerve conduction, although some observers state that a preliminary rise in excitability is their first effect. If not exposed too long to the action of the anæsthetic the nerve will recover; but if too large an amount is used, or if the exposure is too long, irritability and conductivity appear to be permanently lost. Chloroform is much more active than ether and the nerve recovers from it with much greater slowness. This may be due to its being less volatile than ether and hence escaping less readily from the nerve or to its having a more powerful action. The most probable explanation of the action of the anæsthetics is that they dissolve the lecithoproteids or colloids of the nerve. Mayer[35] and Overton[36] have pointed out the parallelism of the anæsthetic action to the fat-dissolving powers of the anæsthetics. The nerve is particularly rich in lecithin compounds, and it is not improbable that the anæsthetics act upon them. The dissolving action of these substances may be easily seen in blood corpuscles, the eggs of many marine forms and other organisms, so that it is probable that they act on nerve protoplasm in the same manner. There is, hence, nothing peculiar about the action of the anæsthetics. They produce the same kind of a change in protoplasm as do positive ions, the positive electrode, or warmth. They put the nerve in a condition of anelectrotonus. They are particularly valuable because they are so soluble in protoplasm, so volatile, and effective in such small amounts.

General Summary.—We are now in a position to see how far the foregoing facts enable us to understand the processes in the nerve which are represented in the nerve impulse. There have been several hypotheses thus far proposed to explain these phenomena. One of the earliest was that of Du Bois-Reymond. In this theory the nerve substance is supposed to be composed of bipolar electrical particles negative at each end and positive in the middle. The current of rest is obtained by connecting the middle or positive surface with the cut end or negative surface. As each portion of a magnet shows the polarity of the whole magnet, so each portion of a nerve shows the polarity of the whole nerve. The nerve impulse is simply a turning of these particles on their axes, so that the negative ends turn toward the surface. This will explain the action current.

Hermann believed that these particles did not pre-exist, but that the current of injury was due to catabolic changes taking place at the cut surface. This became negative to the rest in consequence of these chemical changes. A similar change occurred during conduction, and this change in each part of the nerve caused the part just following it to be put in a position of catelectrotonus. On this theory the negative variation stimulated each part of the nerve in turn and was itself regenerated by the change which it brought about.

Becquerel supposed that there were numerous electrocapillary couples in the nerve which gave rise to electric currents, each couple, consisting of two different liquids, being separated by a capillary opening or by an organic membrane. D'Arsonval, who has developed this theory, supposed the electrical phenomena to be due to modification of the surface of separation of the two liquids similar to the electrical phenomena shown by the capillary electrometer.

Loeb has suggested that conduction is due to a change in state of the colloids, but has furnished no evidence in support of this view. The author believes that the facts indicate the truth of this hypothesis and suggests the following more specific theory:

The protoplasm of the nerve is essentially a colloidal solution. The colloidal particles are proteid in nature and in all likelihood are lecithin proteids resembling the sheaths of the red blood corpuscles, as is indicated by the especial richness of the nerves in lecithin. These particles are of different sizes and are electropositive. They continually change their state of aggregation, being easily precipitated or brought into solution and easily coalescing with their neighbors or breaking up into a large number of smaller particles. Through these changes the surface separating each particle from the surrounding fluid augments or diminishes. When two particles coalesce the total surface is reduced; when one particle separates into two the total surface of separation is increased. Around each particle there are induced in the water electrical changes of an opposite sign. It will be seen that any change in the surface of separation must necessarily produce an electrical disturbance exactly in the same manner as do the movements of the capillary electrometer, and in this respect my suggestion harmonizes entirely with that of D'Arsonval.

Stimulation, whatever its character, whether mechanical, chemical, thermal, or electrical, brings about a change in the state of division of these colloidal particles. It produces either one of two effects, *i.e.*, a coalescence of the particles (gelation), or an increase in number of the particles (solution). According as a stimulus produces one or the other of these effects we say that it excites the nerve or anæsthetizes it. It may fairly be questioned which effect is the excitation and which the anæsthetization. This question may be answered, I believe, by the exciting action of drying the nerve and of applying cold. Both of these processes excite or generate nerve impulses. Since they can hardly be supposed to increase the solubility of the colloids, we may confidently assume that they congeal or precipitate the colloids, and hence that excitation is due to a diminution in the number of colloidal particles and a reduction in their total surfaces; and conversely, anæsthetization or inhibition is due to the reverse process. All the exciting agencies may be interpreted in this way. Thus mechanical shock which disturbs the hydrosol brings about such a condition of temporary coagulation or rigidity of the nerve protoplasm throwing the particles together. This interpretation is strengthened by Mrs. Andrews' observations on the effect of shock on the choano-flagellates, where the rigidity of the previously fluid protoplasm can be easily demonstrated, and by my own observations on other forms of protoplasm, notably eggs. Cold, as will be seen, diminishes the stability of the protoplasmic solution or hydrosol, while warmth increases it; negative ions precipitate positive colloidal solutions and they excite the nerve; excitation takes place at the cathode or negative electrode, where positive colloidal particles will be precipitated; the extraction of water acts in the same manner as cold. In fact all the phenomena of excitation are readily understood on this hypothesis. Similarly the action of all anæsthetizing agents becomes clear. Positive colloidal solutions are rendered more permanent by positive ions, and these annihilate nerve excitability; warmth of moderate amount increases the stability of nearly all solutions, and this diminishes excitability; ether and the anæsthetics dissolve the protoplasm of eggs and other cells and destroy irritability; the anode, which holds positive colloids in solution, abolishes excitability. We may sum up our conclusions in the general law that nerve excitability varies inversely with the stability of the protoplasmic hydrosol. The less stable the hydrosol, the more irritable the nerve. Irritability will be lost when the nerve is stable, either in the condition of solution or in that of total gelation. The rise in irritability at the anode on opening the current is due to the fact that, as already explained, by the action of the current the particles are greatly divided; and after the current is broken the diffusion outward of the positive ions reduces the stability of the hydrosol here and it returns back toward the normal. The electrotonic effects are due to the solution being made more stable near the anode and less stable near the cathode.

As readily as the facts of excitation are understood on this hypothesis, so many of the facts of the electrical phenomena of nerves may be explained. The electrical disturbances are the result of the alterations in the surface of separation of particles and liquid. Whenever these particles coalesce, a portion of the negative charges, formerly induced about each particle, are set free. The portion of the nerve where this is occurring becomes temporarily electronegative to the rest of the nerve. Thus the current of injury is due to the coalescence of particles at the injured end. This is always negative to the uninjured part.

If this is true, the exposure of the end of the nerve to acids or anæsthetics should diminish the current of injury, whereas alkalies should increase it. Such I have found to be the case. The current of action is the result of the progressive precipitation of the colloids and a progressive setting free of negative charges. It is, however, impossible within the limits of this article to discuss the bearing of this hypothesis on all the numerous electrical phenomena of nerves. It may be stated, however, that a warmed or etherized portion of a nerve is electropositive; a cooled portion electronegative to the normal nerve.

The conduction of the nerve impulse may be understood on this hypothesis as follows: Each precipitation of colloidal particles sets free by the accompanying reduction in surface negative charges formerly induced in the water about each particle; these charges at once precipitate the next layer of particles, and so on. Thus the negative variation successively stimulates each following segment of the nerve, as Hermann supposed, and it is regenerated by the change which it itself has produced. The sheath and peculiar structure of the nerve probably, as Boruttau supposes, plays an important part in the electrical phenomena of polarization and stimulation, and possibly in determining the speed of transmission, but the change in the protoplasm itself is the most important factor in conduction. Finally, it should in all fairness be stated that among the difficulties or exceptions to this hypothesis are the statements that the anæsthetics bring about a preliminary rise in irritability, and that conductivity and excitability may vary somewhat independently of each other. Whether these facts can be harmonized with the explanation already offered remains for the present unknown.

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NERVES, PATHOLOGICAL CHANGES IN. See *Neurone, etc.*

NERVE TISSUE, HISTOLOGY OF.—According to the fundamental conception of neurology the entire nervous system, central as well as peripheral, has been regarded as composed of morphological units, the neurones, held together by the supporting tissues, the neuroglia. The term neurone was suggested by Waldeyer in 1891, and was accorded almost universally an international acceptance by anatomists, physiologists, pathologists, and clinicians. The term neura, proposed by Rauber, and neurodendron by Kölliker, to designate the same unit, have not met with similar favor. More recent investigations, however (Apàthy, Betha), have thrown some doubt upon the neurone doctrine as formerly held. The neurone consists of a cell body, dendritic processes, and an axis-cylinder process (axone with its terminal ramifications). As the neurone does not consist only of the cell body, but also has processes, some of which are of extreme length, it is impossible to see the entire neurone in the majority of cases. As a matter of convenience, therefore, the description of the neurone may fall under two headings—the nerve cells or nerve-cell bodies, and the nerve fibres.

THE NERVE CELL.—The essential part of a neurone originating the nerve impulse is the cell body. Nerve cells or ganglion cells, as they are generally called, occur in groups known as ganglia in the cerebrospinal system, the sympathetic system, and in the organs of special sense. While variable in size, they are among the largest cells in the body, often, as in some of the ganglion cells in the anterior horns of the spinal cord, reaching a size of from 90 to 135 μ, the cells of Betz in the paracentral lobule being especially large. Many nerve cells, however, are much smaller in size, the cells of the granular layer of the cerebellum being only from 4 to 8 μ in diameter.

Study of the morphology of the neurones requires the consideration of their external peculiarities as well as of their internal architecture. The former are best revealed by the methods of Golgi and Ehrlich, and the latter by the methods of Nissl and Held.

Morphology of the Nerve Cells.—Nerve cells vary greatly in shape. Starting originally as spherical cells, some may retain this shape as in the spinal, Gasserian, or other ganglia; others may become ellipsoidal, as in the spinal cord, pyriform as the cells of Purkinje in the cerebellum, pyramidal as the cells in the gray matter of the cerebrum, or stellated as the multipolar ganglion cells of the spinal cord. The most conspicuous peculiarity of the nerve cells is the branching. This may take place only on one side leading to a prolongation of the protoplasm into a single pole, such cells being known as unipolar nerve cells; when the protoplasm is prolonged into two, usually opposite, poles, the cells are appropriately designated as bipolar; when the protoplasm extends in several directions multipolar cells are formed. Each polar prolongation is continued to form a nerve-cell process. Of such processes two kinds are recognized, the branched *protoplasmic processes* and the *axis-cylinder process.*

The branched protoplasmic processes, now usually called the *dendrites*, form prolongations of the protoplasm from the cell body, hence the old name of protoplasmic process. They are always broader and thicker at their origin, becoming gradually narrower as they divide,