in the canal. In fact, however, the female at the time of oviposition lives in the lower part of the rectum and even attains the vicinity of the anus, although the earlier portion of the adult life history is passed in the small intestine, where the worms acquire sexual maturity and copulate. Evacuated from the body, the embryo undergoes transformation to the second embryonic stage while still within the egg shell, and now awaits ingestion by a new host. The primary infection is by drinking-water or contaminated fruit or vegetables, which are eaten uncooked; but self-infection and transference to other individuals are brought about by scratching and rubbing with the fingers to allay the intense itching caused by the daily migration of the females out from the anus on to the perineum and the surrounding parts. Perhaps in the distribution of *Oxyuris* eggs the flies play a part such as Grassi has demonstrated for *Trichocephalus* and eggs of *Tænia*. The direct development is very rapid, as Leuckart obtained experimentally *Oxyurides* 6–7 mm. long within fourteen days after ingestion of the eggs; Grassi and others have confirmed this by further experiments.

Pathology.—The females are far more numerous than the males, and by their migrations determine unbearable pruritus, which recurs periodically on retiring. In a number of cases among young girls the worms have migrated into the vagina and have produced onanism, and even the inception of nymphomania. In many cases large numbers in the rectum have excited no untoward symptoms, but in others they have produced reflex nervous activities of all grades up to epileptic attacks, such as have been noted under *Ascaris*. Recent investigations in Egypt have demonstrated the responsibility of this parasite for nodules on the rectal wall, previously attributed to *Schistosoma*, which contain eggs of *Oxyuris vermicularis* in a calculus. *Oxyuris* has also been recorded in tuberculous nodules in the cavum Douglasii of a female, and Vuillemin has recently discovered them in a tumor near the anus of a boy. The latter case shows definitely the wandering of the worms through 2 cm. or more of solid tissue. This habit exhibits a new and evidently dangerous feature in the parasitism of this species through the disturbance of the tissues and the introduction into them of bacteria from the rectum.

Treatment.—It is difficult to remove these worms entirely. Vermifuges and purgatives with enemata, etc., are successful to a degree; but the ease of auto-infection is an obstacle to a complete cure. Local application of mercurial ointment will alleviate the pruritus, and manual extraction, if prolonged, will reduce their numbers rapidly. But in any event treatment is prolonged.

The sub-class of the Gordiacea includes forms familiarly known as "hair snakes" or "hair worms." They are greatly elongated, slender worms, somewhat-filaria-like in external appearance, but of radically different internal structure. Lateral fields are wanting, and the body musculation is of a different histological type from that of the Eunematoda. The mouth is occluded and the alimentary canal persists in the adult only as a functionless vestigial strand. In both sexes the reproductive organs open to the exterior with the alimentary canal at a terminal or subterminal cloaca. The reproductive system is constructed on a different plan, and the lateral canal system is wanting. The male has no spicules, but the posterior end of the body is forked and functions as grasping organ.

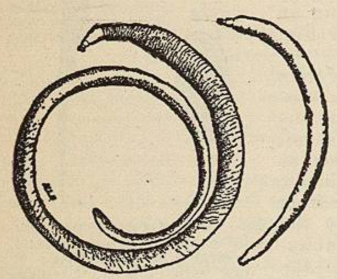
FIG. 3570.—*Gigantorhynchus gigas*. Male at right, female at left. Half natural size. (Original.)

The adult lives free in ponds, swamps, and other bodies of water, and the eggs are deposited on the stems of water plants. The larvæ possess a proboscis armed with hooks and bore into the body cavity of aquicolous insect larvæ, or rarely mollusks, where they encyst. According to Villot the second stage is passed in the intestine and body cavity of fishes. More commonly apparently the worms develop to maturity in the body cavity of insects, from which they emerge into the water for the adult free existence.

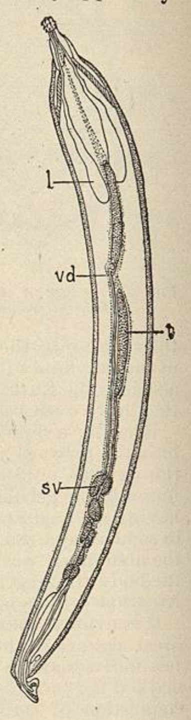

FIG. 3571.—*Gigantorhynchus gigas* Opened to Show Internal Anatomy, *l*, Lemniscus; *sv*, seminal vesicle; *t*, testis; *vd*, vas deferens. Modified. (Original.)

Several species have been reported from the human alimentary canal. They are pseudoparasites, having been swallowed, according to one view, in the adult condition with drinking-water; but their occurrence in fruit, especially apples, makes this even a more likely source of infection. Lockwood noted in 1876 the frequent presence, in fruit, of *Mermis*, another genus of Eunematoda, and suggested the probable occurrence of this form as a pseudoparasite of man under conditions; this has not been actually recorded so far as I find. But of Gordius as a pseudoparasite Parona has recently listed eleven cases, the first as early as 1638; of these Kirtland's (Ohio) is the only one from the United States. Two other unpublished cases have recently been communicated to me from Michigan and Maryland. It will be of no particular value to enter here upon a detailed description of the species found.

The Gordiacea are, however, emphasized by Cobbold as important for the medical practitioner, since they have been passed off as the guinea-worm and as having been evacuated with fecal matter by neurasthenic persons under treatment.

The Acanthocephala may best be discussed as an appendix to the class Nematoda, although they are regarded by many as a cognate class and by others are separated even more widely. The forms included here, though parasites of the most complete type, are not common in man. The group may be characterized as follows: Elongated, cylindrical body, often deeply corrugated, bearing at anterior end a retractile proboscis provided with many minute hooks in rows. No trace of alimentary canal. Reproductive organs open at posterior end; sexes separate. Male with campanulate bursa about the orifice. Mostly small forms, parasitic as adults in vertebrates only. The structure is uniform, and can be learned from the brief account which follows of the largest and commonest species.

Gigantorhynchus gigas Hamann 1892.—(Syn.: *Tænia hirudinacea* Pallas 1781; *Echinorhynchus gigas* Goeze 1782.)

Body milk white, sometimes slightly tinted, with transverse irregular ridges. Posterior end somewhat smaller; proboscis spherical, armed with five or six rows of hooks. The proboscis can be retracted into a neck-like region, which is much slimmer than the following portion of the body. Male, 60–90 mm. long by 3–5 mm. broad, with bell-shaped caudal pouch. Female, 230–350 mm. long by 4–9 mm. broad; tail blunt; eggs almost cylindrical, 0.087–0.1 mm. long with three embryonic envelopes.

The adult worm is found in the small intestine of the pig, ordinarily fixed to the wall by the proboscis, and is widely distributed.

Structure.—The elongated body (Fig. 3570) is largest near the head and tapers gradually toward the posterior end. At the anterior end a sharp constriction separates the body from the short neck portion, which is not more than one-fourth or one-fifth the diameter of the body close to it. From the apex of this region may be projected the proboscis which is contained within it, like the reversed finger of a glove. As the proboscis rolls out the hooks also turn outward, and when the proboscis is completely extruded the shape of the organ is nearly that of a sphere on which are from five to six irregular rows of hooks. Behind these the proboscis is slightly smaller.

If the internal structure be examined, it will be seen that the proboscis is provided with retractor muscles, by means of which it may be withdrawn into the body. At the base of the proboscis is the small mass of nervous matter which represents the brain.

There is no trace of an alimentary canal, hence these forms, like the tapeworm, take nourishment by absorption. Two elongated sac-like organs hang down into the body cavity along the sides of the proboscis. These are the lemnisci (*l*, Fig. 3571); their function is uncertain.

The mass of the body is made up of the organs of the reproductive system. All these worms are diœcious. The male organs (Fig. 3571) consist of two large testes, together with the ducts and accessory glands connected with them. The tail of the male has a hemispherical expansion, something like the caudal bursa of other Nematoda; the male sexual opening in the centre of this sac at the tip of the body is provided with a small copulatory organ. The internal sexual organs of the female are much similar in general appearance; the ovaries lie toward the front of the body cavity, which is largely filled with eggs in various stages of development. These are discharged by the oviduct, which opens at the posterior end of the body.

Life History.—The eggs of *Gigantorynchus* are discharged from the alimentary canal of the host and distributed with fæces. When eaten by some insect they are hatched in its intestine. The embryo, which has a conical form armed at one end with four hooks like tapeworm hooks, and a number of smaller ones, penetrates into the abdominal cavity of the insect and encysts there. In this condition the embryos may even live through the metamorphoses of the insect until the host is eaten by some pig. In the alimentary canal of the pig the embryo is set free, attaches itself and acquires maturity. There is some dispute as to what insect is the intermediate host; the white worm-like larva of the May bug and the larva of the common rose chafer have been found to contain these worms in Europe, and Stiles has experimentally infected the larvæ of the June bug in this country. It is also maintained that various species of snail may function as the larval host. In all probability the larva is not confined to a single host, but may develop in many.

Leuckart accepts some reports of the occurrence of this species in man as trustworthy, and Lindemann says that it is not rare as a human parasite in Southern Russia. Schneider notes the consumption, as food, of the larvæ and adults of *Melalontha*, the May beetle, which acts as the intermediate host, so that infection is evidently possible.

Gigantorhynchus moniliformis (Bremser 1819).—Body attenuated anteriorly. Proboscis, 0.425–0.450 mm. long, 0.175–0.19 mm. broad, with hooks in fifteen transverse and twelve longitudinal rows. Male, 4–4.5 cm. long. Female, 7–8 cm. long, or even up to 27 cm., according to Westrumb. Eggs ellipsoidal, 85 μ long, 45 μ broad.

The normal hosts of this species are field mice, rats, etc., and the intermediate host in Italy has been determined as *Blaps mucronata*. Calandruccio in experimenting on the life history succeeded in infecting himself with the adult. The severe symptoms which manifested themselves were dispelled by the evacuation of the worms. In other cases of the occurrence of this species as a human parasite its identity was less definitely established.

Echinorhynchus hominis Lambl 1859.—Length, 5.6 mm.; width, 0.6 mm.; proboscis almost spherical with twelve transverse rows of eight hooks each. Large hooks, 103 μ long, small hooks, 77 μ.

An uncertain species of which Lambl found a single specimen at Prague in the small intestine of a boy who had died of leukæmia.

Echinorhynchus sp. Welch 1872.—In 1872 Welch described as *Echinorhynchus* a body which he found encysted in the mucosa of the jejunum of a soldier. According to Railliet it was evidently a Linguatulid (see *Arachnida*).

Echinorhynchus sp. Moniez 1896.—Kunstler and Pitres found certain peculiar bodies in the pleural cavity of a patient who had suffered two years from pleurisy, but without fever. They interpreted these structures as coccidia, but Moniez holds with greater probability to their likeness to eggs of *Echinorhynchus*. The case is entirely isolated under either explanation.

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NEOPLASMS. See *Tumors.*

NEPHRECTOMY; NEPHROTOMY. See *Kidneys, etc.*

NERVES, GENERAL PHYSIOLOGY OF.—HISTOLOGICAL AND GENERAL.—Nerves consist essentially of the long, slender processes of nerve cells. They are hence composed of protoplasm, and they possess the general chemical and physical properties of this substance; but they differ physiologically from other forms of protoplasm, in that they possess to a high degree the properties of conductivity and excitability, while the properties of growth, metabolism, respiration, and contractility are feebly developed or altogether absent. There is in these respects a marked physiological difference even between the nerve and the cell body from which it arises. Many of the reactions of the cells to external conditions are the opposite to the reactions of the nerve. The cell generates nerve impulses; it possesses spontaneity or automatism, absent in the fibre; it is closely dependent on a supply of oxygen, while the nerve is almost independent; it has an active metabolism, which the nerve lacks almost entirely; it respires, while the nerve respires little or not at all; it or some of its dendritic processes may be contractile, the nerve has lost this property altogether. The physiology of the nervous tissue, which includes nerve cells, differs therefore in many respects from that of the nerves proper, which we shall consider here. In short, the nerve cells possess pre-eminently the property of automatism or spontaneity; the nerve fibre, the property of conduction.

This physiological differentiation of the conducting protoplasm of the nerve is accompanied, as might be expected, by an histological differentiation. The protoplasm of the nerve fibre, called the axis cylinder, or axon, differs in physical appearance from that of the rest of the cell body from which it is derived, in that the fibre is striated longitudinally as if composed of distinct fibrils, and is surrounded by a fatty sheath. These fibrils can be more easily seen in invertebrate than in vertebrate nerves, and particularly in the leeches, where they have been traced by Apathy[1] from one nerve cell into and even through other nerve cells. Some observers even go so far as to maintain that these fibrils are the true conducting portions of the fibre, but of this there is no physiological evidence. Besides this peculiar fibrillar structure of the axis cylinder, nerves are as a rule easily differentiated from other tissues even by the naked eye by their white, glistening, fatty sheaths. Nearly all nerve fibres which take their origin in the brain and spinal cord, and many having origin elsewhere, are surrounded by such a sheath, which is called the medulla, and such nerves are called medullated nerves. The nerves of invertebrates and those of the sympathetic system of vertebrates, on the other hand, often lack these sheaths, and are called non-medullated nerves. The function of this medullated sheath is not definitely ascertained, but it has been suggested that it prevents the spreading of the impulse from one fibre to another. It appears to influence the physiological behavior of the nerve, for medullated nerves are generally more easily excited than non-medullated, and they react differently to an exposure to a constant electrical current. A momentary exposure of a non-medullated nerve to a constant electrical current may block conduction in the region of the anode or positive electrode for several minutes or hours; whereas medullated nerves after such treatment recover their conductivity very quickly.[38] Waller[2] suggested that the medulla was reserve material which was used up by the metabolism of the nerve during conduction, and he explained in this way the indefatigability which medullated nerves possess; but Miss Sowton[3] has recently shown that the non-medullated olfactory nerve of fishes is almost or quite as inexhaustible as are medullated nerves, if we may judge from the undiminished size of the electrical response attending conduction after long stimulation. Nerve fibres differ from other protoplasm also in the quickness with which they stain blue when exposed to a solution of methylene blue. It is thus possible to stain them before the other tissues are colored, and an important method for tracing the course and distribution of nerves has been founded on this peculiarity.

The chemical composition of the axis-cylinder process is not definitely known. Other portions of gray nervous matter which it resembles consist largely of colloidal substances of proteid nature, and differ from most tissues in the unusually large amounts of lecithin and cholesterin present. Nothing can be said positively regarding the inorganic salts present in the axis-cylinder process. Ranke[4] believed its reaction to be slightly acid, but most observers have found the cut surface of the nerve alkaline to litmus; it is possible that like other protoplasm it is neutral to phenolphthalein. The medulla consists chiefly of cerebrin, lecithin, cephalin, cholesterin, and neurokeratin. The latter substance forms a horny supporting framework. Lecithin is a trimethyl cholin-distearyl phosphoric acid glycerin ester. Other fatty acids may be present in place of the stearic acid, and the lecithins from different animals vary in this respect. The kephalin or cephalin, according to Koch and Thudicum, is probably monomethyl cholin lecithin. The constitution of cerebrin is unknown, but in the brain of the sheep it contains the sugar galactose, two or four molecules of stearic or oleic acid containing nitrogen, possibly united to a hexatomic alcohol or to glycerin. The cerebrins obtained from the brains of different animals differ chemically. The high content of all nerve tissues in lecithin and cholesterin is probably of physiological importance, as will be shown farther on, and possibly determines their susceptibility to the anæsthetics.

As the conducting part of a nerve fibre consists of protoplasm, it cannot continue to exist for any length of time if cut off from the rest of the cell, but soon degenerates and disintegrates. Experiments on plant cells and infusoria have shown that portions of the cell cut away from the nucleus die and no longer grow, although they may continue movement and some other functions for some days.[5] The nerve fibre shows the same relationship, demonstrating that its maintenance in a normal condition depends on its connection with a nucleated part of the cell body. If a mammalian nerve is severed, the peripheral portion, whether sensory or motor, loses its power of conduction and excitability in from four to six days.[9] In frogs conduction may persist for from five to eight days, and, in nerves kept cool, even longer. These facts indicate that the nerve fibre, however close its connection with the peripheral cell which it innervates, is not nourished from it and does not enter into organic connection with it; and, further, that it is not nourished by the nuclei of the medullary sheath. No immediate functional reunion of the peripheral and the central ends of a severed nerve can be brought about by suturing, for whether sutured or not degeneration of the peripheral part always occurs. This is accompanied by the division of the nuclei of the medulla and the fragmentation and fatty degeneration of the axis cylinder and medullary sheath. Degeneration does not extend gradually downward from the cut end of the fibre, but takes place with the same rapidity in the whole of the cut-off portion. The restoral of function in the cut nerve is brought about by the growth downward of the central ends of the cut fibres—of those fibres, in other words, still in connection with the nerve cells.[6] These push down in the paths of the degenerating fibres and ultimately become medullated and re-establish union with the peripheral organs, although this may be prevented if the fibres meet in their course any obstacle which turns them aside. There appears to be no choice of termination on the part of the fibre—for example, of a motor fibre for a muscle cell or of a sensory fibre for a sensory end-organ—for if the central end of a sensory nerve is sutured to the peripheral end of a cut motor nerve, the sensory fibres will innervate the muscle fibres formerly supplied by the motor nerve, and vice versa.[7] Also if the vagus and sympathetic be cut and the central end of the vagus cross-sutured with the upper end of the sympathetic in the neck, the vagus fibres growing upward in the paths of the degenerating sympathetic innervate the submaxillary gland and cause secretion on stimulation, and thus take on a secretory function.[8] Similar facts have been established by Langley for the fibres innervating the pupil and those erecting the hairs on the cat's neck, and by Cunningham and other observers in other nerves. The time required for the restoration of the function of the nerve will depend in part on the distance the nerve has to grow to re-establish union, and in part on the nerve which is regenerating. The longer the distance which the regenerating fibre has to grow before reaching its destination, the longer will be the time required for regeneration. On the other hand, nerves differ somewhat in their speed of regeneration or growth, and no doubt constitutional differences of this sort exist among different individuals. The time required is as a rule from two weeks to four or more months. For some reason the nerve fibres within the cord appear in mammals to have little power of regeneration if the cord is severed. The reason for this peculiar reaction is not yet satisfactorily explained. The subject is badly in need of careful investigation, since even the possibility of regeneration in mammals is not definitely disproved.[10]

Excitability.—Nerves are excitable—that is, they will respond to stimulation, at any point in the course of the fibre. No variation in excitability at different points of the nerve has been detected in any one nerve as long as it remains uninjured in the body,[11] but if the nerve is injured by cutting it or its branches, an increase of excitability is brought about in the immediate neighborhood of the injury.[12] This increase in irritability is probably due to the electrical disturbance set up in the nerve by the injury and called the current of rest. This apparent variation in excitability, really brought about by injury following the cutting of branches of the nerve, has been described by Grützner and others, and was at first interpreted as showing variations in irritability in the normal nerve. It is easily demonstrated in the frog's sciatic in the neighborhood of the branches given off to the thigh muscles. The region of increased excitability extends about 5–7 mm. along the nerve from the point of injury.[12] While there is no variation in excitability in the same nerve, there is a considerable variation between the different motor nerves of the same animals, those nerves most frequently used appearing as a rule to be the most easily excited. Thus the sciatic nerve of the frog is far more irritable than the brachial nerve to all kinds of stimuli,[13] and sympathetic fibres appear less excitable than motor.

The change in the nerve which gives rise to the nerve impulse, *i.e.*, the excitatory change, may be caused in any one of the following ways: (1) By mechanical shock; (2) by heat of 38° C. or above; (3) by lowering the temperature of the nerve to +3° or −2° C.; (4) by taking water from the nerve; (5) by the action of specific chemical substances; (6) by electrical currents; and (7) by ether vibrations.

Mechanical Stimulation.—Mechanical stimulation, first discovered by Swammerdam[14] about 1650, may be brought about either by suddenly stretching the nerve, by shaking it, or by a sharp blow. Pressure gradually increased does not excite the nerve, though it at first increases its excitability.[15] Mechanical stimulation is seldom used in experimentation, as the nerve is generally crushed or injured by repeated shocks; but special appliances have been developed to avoid this so far as possible. Among these are the tetanomotor of Heidenhain[17] and the apparatus of Uexküll,[16] the former instrument delivering a series of sharp blows; the latter shaking the nerve. The excitability of nerves to mechanical stimulation varies greatly, and may be artificially increased or diminished. Thus the extraction of water from the nerve may render the latter so sensitive to mechanical stimulation that the slightest jar, or the lightest touch of the nerve with a glass rod will cause the discharge of a series of nerve impulses, causing tetanus of the attached muscle. The time relations of the stimulus and the resulting contraction are the same with mechanical and electrical stimulation. After a few blows a nerve may become non-irritable to further stimulation, but if left undisturbed it slowly recovers.[11]

Heat Stimulation.—A moderate degree of warmth (10°–25° C.) diminishes nerve excitability. To cause the generation of a nerve impulse by heat the nerve must be heated suddenly to a temperature of 38° C. or higher. Heating a nerve quickly from 3° C. to 20° C. does not generate a nerve impulse. These facts show that it is not a sudden increase in heat or change in temperature of the nerve which stimulates, but the exposure of the nerve to a certain critical temperature; and this suggests that probably heat stimulates by coagulating some of the proteids of the nerve. This conclusion is supported by the fact that if the nerve is kept at 40° C. for a short time it loses its irritability permanently, although if it is exposed for a few moments only, an impulse may be generated and excitability restored if it is again cooled; and by the further fact that the temperature at which a nerve is stimulated by heat is about the temperature of coagulation of a proteid isolated by Halliburton from brain tissues, *i.e.*, 35°-40° C. The restoral of irritability on recooling sometimes observed after a short exposure to 40°–45° C., is apparently opposed to the hypothesis that heat stimulation is due to coagulation; but this restoral may be owing to the coagulation having been but partial.

Cold Stimulation.—If the sciatic nerve of the frog is exposed to a temperature of 3° C. or lower, tetanus of the attached gastrocnemius muscle generally follows.[18] Cooling the nerve from 20° to 3° C. increases the excitability of the nerve to all stimuli, but does not as a rule generate nerve impulses sufficiently strong to produce muscular contraction. The cooling tetanus resembles that produced by drying the nerve, and there is thus a similarity between the physiological effects produced by cooling and those produced by the extraction of water, resembling that emphasized by Greeley in connection with the production of spores in infusoria. Below 0° C. or −2° C. the frog's nerve loses its irritability, but may be restored by very cautious warming. Mammalian nerves, according to Howell and others, lose their conductivity at 5° C., or even at a higher temperature, without preliminary stimulation.[19] It has been suggested that the tetanus produced by cold is due to mechanical stimulation by the ice crystals formed; but this is not probable, since the nerve may be stimulated at a temperature above the freezing point of the nerve, and the gradual rise in excitability as temperature is lowered shows that the final stimulation is but a culmination of a process going on as temperature falls. The increase in excitability produced by cold is true also for mammalian nerves (Biedermann). Conductivity, on the other hand, is reduced by cold. Not only does cooling increase the excitability of the nerve fibre, but the whole central nervous system may in the frog be brought by this means into a condition of increased reflex excitability resembling that caused by strychnine.[37] The increase of excitability produced by cooling culminating in stimulation may be compared to the precipitation of moisture from the atmosphere, and, as will be discussed on page 232, may be brought into relation with the change in state of the colloids in the nerve.

Drying Stimulation.—If nerves are allowed to dry in the air they gradually increase in excitability, and finally nerve impulses are generated sufficient, in the case of motor nerves, to cause a prolonged tetanus or series of twitches of the attached muscle. The dried nerve, like the cooled nerve, becomes totally non-irritable and very stiff, but its excitability may be completely restored by placing it in water or physiological salt solution. A similar drying tetanus is produced by placing the nerve in solutions of sugar, urea, glycerin, or other non-electrolytes having an osmotic pressure of thirteen atmospheres or over, that is, in solutions containing something more than a half-gram molecule of the substance to the litre, or by placing it in solutions of neutral salts of the same osmotic strength. Even neutral salts which by their own action annihilate nerve irritability will stimulate if strong enough to extract water rapidly. The stimulating action of solutions of nearly all non-electrolytes and many electrolytes except sodium salts and a few other compounds to be discussed later, is to be explained by the indirect osmotic extraction of water. If the water is extracted very gradually the nerve may be dried without generating impulses strong enough to cause muscle contractions. It has been suggested (Grützner) that this stimulation is really mechanical, due to shock or compression of the nerve substance by the shrinking tissue, but this is probably not the case. A probable explanation of this stimulation will be found on page 232 and may be confidently ascribed to a change in the nerve similar to that produced by cold.

Chemical Stimulation.—The excitation of the nerve by chemicals was first observed by Swammerdam in the seventeenth century. It has been studied by von Humboldt, Eckhard, Kölliker, Kühne, Grützner[20] and many others. The earlier work established the general fact that the application of solutions of many non-electrolytes and electrolytes would stimulate motor and sensory nerves. The strong solutions which were used led to the conclusion that most chemicals stimulated indirectly by the withdrawal of water, a conclusion which was undoubtedly correct. The first careful work comparing solutions containing the same number of molecules in the litre was done by Grützner, who showed that some other factor entered into the stimulation besides the withdrawal of water. He was unable to discover what this was, but referred it to a specific stimulating action of the salts. Thus sodium fluoride and other sodium salts and some alkalies stimulated in solutions too weak to draw water from the nerve. Grützner found that with certain exceptions a relation existed between molecular weight and stimulating or poisonous action. In salts of the same series those of greater molecular weight stimulated more and poisoned more rapidly. Thus sodium iodide was stronger than the bromide, and this than the chloride. Barium chloride was more baneful than strontium chloride. Grützner believed that sensory nerves were more readily stimulated by potassium salts than by sodium, while motor nerves were not stimulated by potassium salts, but were by sodium. This conclusion is not correct. The author's observations[21] on a large number of salts, acids, and alkalies gave the following results: The frog's sciatic is stimulated by immersion in solutions of any salt, if this be sufficiently concentrated. This stimulation, as already stated, is brought about osmotically. If the solutions have an osmotic pressure no greater than that of the nerve—*i.e.*, approximately six atmospheres—only solutions of electrolytes will stimulate; the non-electrolytes are ineffective. Of these electrolytes all sodium salts of monovalent or bivalent acids, with one or two possible exceptions, will stimulate in isotonic solutions. The similar salts of other metals, such as potassium, lithium, calcium, strontium, magnesium, zinc, silver, mercury, aluminum, iron, and ammonium, will not stimulate, but gradually annihilate irritability. Of the sodium salts the monovalent salts, such as the chloride, bromide, iodide, nitrate, and acetate, are least powerful; the bivalent salts, such as the sulphate, oxalate, tartrate, and borate, are from two to three times as powerful as the monovalent; while the trivalent salts, such as the citrate, ferro- and ferricyanides, and the phosphate, are about six times as powerful as the monovalent salts. This shows that the stimulation is due to the anion and not to the cathions, and further, that it is dependent in part upon the number of electrical charges on the anion. In other words, chemical stimulation is really due to the negative electrical charges of the salt, and chemical stimulation is an electrical stimulation. The positive ions have an effect opposite to that of the anions, and tend to prevent stimulation and lower irritability, and this is due to the positive electrical charges which they bear. Thus potassium, lithium, ammonium, and hydrogen not only will not stimulate the nerve except in strong solutions or when united to still more powerful trivalent anions, but they annihilate nerve irritability very rapidly. All acids destroy nerve irritability rapidly unless applied in very dilute solutions. In some acid salts, however, such as copper sulphate, a nerve may remain highly irritable for several hours. In solutions having a strength of one-fifth normal or higher, acids will often stimulate (osmosis ?), but below this strength they annihilate irritability. Of the alkalies, sodium, potassium, and barium hydrates stimulate in dilutions not greater than one-twentieth normal; ammonium hydrate will not stimulate the motor nerve, but destroys its irritability. This is in harmony with the small dissociation of the compound. Of the oxidizing salts the permanganates will stimulate both in the case of potassium and in that of sodium, in one-twelfth or one-fourteenth molecular solutions. Of the monovalent sodium salts the fluoride, iodide, bromide, and chloride stimulate in the order named, the fluoride being the strongest. Something besides the number of charges is thus seen to be of importance. The author has suggested that this is the movement of the charges about the atom, but this is as yet hypothetical. The general result of this work is that positive and negative ions act as a rule in an opposite manner, and that chemical stimulation proper, as apart from stimulation by osmosis, is in reality an electrical stimulation and produces the same kind of a change in the nerve as does electrical stimulation.

Electrical Stimulation.—Nerves may be stimulated electrically in several ways, but the end result is a disturbance of the electric equilibrium, if we may so term it, within the nerve and a resulting change in the nerve itself which causes the nerve impulse. One way, as has just been shown, is to introduce the electrical charges into the nerve in the form of ions in solution, but the more usual method of stimulation is to change the distribution of charged particles already in the nerve and thus upset electrical equilibrium. The nerve may be stimulated by induction by bringing near the nerve a highly charged Leyden jar and suddenly discharging the jar, or, as in unipolar stimulation, by connecting the nerve with one pole of an induction coil, when on making and breaking the primary circuit stimulation may ensue.[22] In both these cases, at the moment of making or breaking the current, there is a sudden equalization of the charges which have been accumulated in the nerve by induction. In other words, the electrical equilibrium is upset by induction. Herz waves may stimulate a nerve which is near the induction machine, but the nerve quickly loses its irritability and conductivity under their influence.[23] The exact manner of action of the Herz waves has not been clearly determined. Induced currents from the inductorium and constant currents from the battery are the forms of electrical stimulation most generally used. Both these currents stimulate in the same way, the differences between them being due only to differences in intensity and duration of the current. The most probable explanation of their action, speaking in general terms, is that they alter the distribution of ions in the nerve, the negativity of the nerve being increased in the neighborhood of the cathode owing to the predominance here of negative ions and the positivity in the neighborhood of the anode. In this way a disturbance of electrical equilibrium within the nerve is produced. It appears that to bring about this disturbance of equilibrium with sufficient suddenness to cause a nerve impulse, polarization must take place in the nerve. This polarization is due to the fact that the membranes surrounding the axis-cylinder process do not permit free osmosis of the salt particles in the nerve through them. It thus happens that when a cathode is brought against a nerve, the negative ions which are repelled from it or are diffusing into the nerve from it accumulate against the outside of the membrane lining the axis-cylinder process. This accumulation of negative particles on the outside of the membrane holds bound to it on the inside the positively charged sodium particles or other positive ions in the nerve in that region. This disturbs the electrical equilibrium of that part of the nerve, as it leaves a surplus of unbound negative charges in the nerve at that point. It is this sudden surplus of negative charges which sets up in the nerve that change which causes the nerve impulse. What the nature of that change is we shall shortly discuss, but it may be said here that it consists possibly in a change in the nature of a precipitation taking place in the colloids of the nerve, strictly analogous to the changes produced by cold or by the extraction of water.

A study of the phenomena of electrical stimulation has led to the general law that that form of electrical stimulation is the most effective in which the intensity of current is greatest and reached in the shortest time.[22] In other words, stimulating power is a function of the intensity and of the reciprocal of the time. For this reason sharp shocks of great intensity, such as induction shocks, are more efficient than the galvanic current, and the break-induction shock is more powerful than the make, as in the latter the rise is more gradual owing to self-induction in the primary coil. Too rapidly repeated shocks will not stimulate, and at 15° C. a duration of 0.0015 to 0.02 second is necessary. Shocks more rapid than three thousand per second generally cause but a single initial muscle twitch.

It has been shown that the nerve impulse does not arise throughout that portion of the nerve which is traversed by the current, but only at its point of exit and entry. The point of entry of the current into the fibre is called the physiological anode, and that of exit is called the physiological cathode. The impulse is formed at the cathode on making the current and at the anode on breaking it.

This may be easily demonstrated by ligaturing the nerve between the electrodes so as to interrupt the conduction of a nerve impulse at this point, when it will be found that the muscle will contract only at the making of the current when the cathode is on the muscle side of the ligature and at the break of the current when the anode is on the muscle side of the ligature. It is a curious fact that if either electrode is placed on a portion of the nerve which has been rendered non-irritable by ether or in any other way, the impulse which normally is produced by that electrode no longer appears. It looks as if the passage of the current from a non-irritable to an irritable portion of the nerve will not stimulate. The reason for this fact of polar failure is still obscure. Electrical stimulation taking place at the cathode at the make of the current is thus shown to correspond to chemical stimulation. It is always an increase in the number or efficiency of the negative ions or a diminution in the number or efficiency of positive ions which stimulates. The positive electrode, as we shall see, diminishes excitability like the positive ions. It makes no difference whether the charges are applied to the nerve on atoms in the form of ions, or from a battery, the effect on the nerve is the same. Electrical stimulation quickly exhausts the excitability of the nerve at the point stimulated, unless the current is frequently reversed. This exhaustion is frequently attributed to electrolysis; but as it occurs also with non-polarizable electrodes, it is due not to electrolysis but to changes brought about in the condition of the nerve, or, more properly speaking, its colloidal particles, by the changed distribution of ions in the nerve. In using the induction shocks where reversal of the current occurs with every make and break shock, exhaustion is far less apt to happen than when a constant current is used.

The action of electrical currents on the nerve does not end with the initial stimulation but continues during their passage, and will be discussed later under the heading of electrotonus. Suffice it to say here that under ordinary circumstances, and unless the excitability of the nerve has been artificially increased by local cooling in the neighborhood of one electrode, or by drying, or by the chemical action of sodium chloride or other substances, the current generates a nerve impulse large enough to cause muscle contraction only at the moment of opening and closing the circuit. If, however, the local excitability of the nerve is increased in the neighborhood of one of the electrodes in any of the above ways, a series of nerve impulses causing tetanus may be produced, lasting throughout the passage of the current or occurring after its close.

Modification of Excitability.—The excitability of a nerve at any point may be artificially increased or diminished. The local application of cold increases excitability down to about +2° C. for the frog's nerve and somewhat higher for the mammalian. Below this point excitability rapidly falls. Local warming diminishes excitability until a temperature of about 35° C. is reached, when excitability again increases. The excitability of the nerve is increased by local injury such as section, or mechanical pressure, or heat action. For about 5 mm. from the cut end of a nerve this increase in excitability is well marked. This increase may be due to the electrical disturbance or current of injury in the neighborhood of the injured part, a condition of catelectrotonus prevailing at this point. In all electrical stimulation the disturbing influence of this nerve current has to be considered. The local application of alcohol, ether, carbon dioxide, or chloroform is said to increase excitability at first (Waller) before anæsthetization takes place. Waller observed an increase in the size of the negative variation when these agents were used. It is not impossible, however, that it is the conductivity which is altered, the general analogy between the effects of these agencies and moderate warmth elsewhere strengthening this supposition. Excitability is enormously increased by drying the nerve, or by taking water from it by osmosis. It is increased further, temporarily at least, by allowing the nerve to lie in one-seventh normal sodium-chloride solution, or by a brief exposure to the sulphate, citrate, or other stimulating sodium salts, and it is diminished by hydrogen, potassium, lithium, ammonium, calcium, and other positive ions. Distilled water at first increases excitability and then diminishes it. Excitability is also powerfully influenced by the passage of a constant current through the nerve, being greatly reduced in the region of the anode and increased in the neighborhood of the cathode while a current of moderate intensity flows through the nerve. Excitability increases in the neighborhood of the anode on breaking the current. The changes in excitability thus produced will be discussed under the heading of Electrotonus.

SUMMARY.—*Excitability.*—The facts concerning excitability just stated are most readily interpreted by assuming that all the agencies which stimulate or increase excitability do so by producing the same sort of a change in the nerve protoplasm. What that change is we are not yet in a position to state definitely; but the many striking resemblances of the process to the reactions shown by colloidal solutions strongly indicate something more than a passing similarity between the two processes. The facts may be conveniently interpreted if we assume the nerve to consist of electropositive colloidal particles and stimulation to consist in the coalescence or gelation of these particles. The action of cold, of mechanical shock, of negative ions, and of the negative electrode in stimulating may on this hypothesis be easily reconciled, all of these agencies acting in the way specified to produce gelation. This matter will be considered at the end of the article more in detail. The various agencies which diminish excitability diminish the tendency of the particles to coalesce.

Conductivity.—The principal function of a nerve is the conduction of a nerve impulse. Conductivity is not something peculiar to the nerve, but is found in all protoplasm. In the sensitive plants, for example, in the absence of nerves an impulse is propagated from place to place through the cells at a fairly rapid speed. This observation allows us to disregard at once such elements as the medullary sheath or longitudinal fibrillæ of the nerve as unessential in the matter of conduction. As protoplasm without these structures still conducts, it is clear that whatever rôle they may play in determining other factors of conduction, for example speed, they are not essential to conduction itself. Conduction takes place in any nerve in either direction with the same ease. Thus if a nerve is stimulated in the middle the impulse passes both downward and upward and may be detected by the negative variation or electrical disturbance which the nerve undergoes. The effect of this impulse passing downward in a motor nerve is apparent in the muscle contraction; what effect the impulse passing upward to the motor cell may have is not yet determined. The rate of conduction varies in different nerves. It is highest in mammalian nerves and in the frog's sciatic, *i.e.*, 25 to 40 metres per second. In the lobster it travels 6 metres per second; in the mollusc, Anodon, only 1 cm. per second; in the mantel of Eledone 1 mm.; and in the electric nerves of the Torpedo at 5° C. 9 metres per second. At a higher temperature Schönlein found a rate of from 12 to 27 metres per second.[24] In the plant Dionæ, conduction, according to Burdon Sanderson, occurs at the rate of about 200 mm. per second at 30°–32° C. No optical changes have been observed in the nerve accompanying the passage of the impulse, but in the insectivorous plant Drosera and in other plants Darwin observed that the passage of the impulse was accompanied by the appearance of a cloudy precipitate in the cell protoplasm, this precipitate shortly dissolving. This precipitation he called aggregation and compared it to the nerve impulse.

Influence of Temperature.—The speed and character of the nerve impulse are influenced by temperature. Bernstein observed an increase in the height of the muscle contraction if the impulse passed through a warmed area. Howell and Budgett secured similar results in the vaso-constrictor mammalian nerves. Waller found that