and nervous vigor and self-confidence that they become more deeply implicated the more they struggle to free themselves, the rejuvenation often secured through this means is remarkable. For some of them, it is the moral element in the "cure" which is the most important, for others the opportunity for nutritive improvement.

The "rest-cure" consists of several parts—seclusion, generally with removal from home and complete rest in bed, during six or eight weeks; forced feeding, massage, and electricity. This system may be modified or simplified to suit special needs, but in severe cases there is no part of it that can be safely omitted. The complete removal from responsibility and care, from unhealthy and familiar surroundings, the anxiety of friends, and most of all, from a vague sense of responsibility as regards themselves, which the enforced rest involves, gives a feeling of mental repose, like that afforded by a long sea voyage to a person simply fatigued by overwork.

The *food* consists at first of skimmed milk,* given in small quantities every two hours, and rapidly increased until the patient takes two quarts daily. Solid meals are then gradually added, so that soon the patient is taking a very large quantity of nourishment, and in the absence of all other calls upon his nervous strength, digests it perfectly well.

Massage† is given once, or even twice, daily, taking the place of voluntary exercise. The latter is absolutely forbidden, even to the extent of feeding one's self, with the result that the patient, having no excuse for feeling tired, soon loses even the apprehension of fatigue. After a time muscular exercises are added to the massage, and eventually substituted for it, and the patient is gradually allowed to walk.

As the patient is obliged to lie constantly in bed, it is important that her time should be sufficiently occupied, and this is not difficult, especially if she has a private nurse of the proper temperament and experience.

The following was the daily schedule of a patient of the writer's, and may be taken as a typical specimen: 7 A.M., small cup of black coffee; patient allowed to brush her teeth. 7:45—Hands and face washed, fire made by nurse. 8—Breakfast, which at this time consisted mainly of a pint of gruel (taken slowly, and kept warm when desired, by table-lamp). 8:30—Sponge bath; bed made. 9:30—Windows open for half an hour (the weather being cold the patient was warmly covered except for the face. 10—Breathing exercises; food. 10:30—Hands and feet exercise, following by reading aloud for fifteen minutes, 11:30—Temperature of body taken, and patient rolled in blankets. 12—Food. 12:30—Bath given. 1 P.M.—Massage and rest. 3—Hair brushed, reading aloud. 4—Food; breathing exercises. 7—Hands and feet exercise; patient arranged for the night. 8—Food. 10—Food.

In some cases we have given patients breathing exercises to carry out every hour or two; and, as a commencement of more vigorous exertion, have had them roll over from one side of the bed to the other a certain number of times. These hints from personal experience are offered, not as constituting material modifications of the treatment as laid down by Dr. Mitchell, but as likely to prove useful where the full treatment cannot be carried out, which so often happens.

The cases which are the most benefited by the rest-cure are those in which the nervous symptoms are caused or maintained mainly by simple anæmia or impaired nutrition. Even in the purely "nervous" cases, however, an occasional treatment of this kind often gives a chance to start fresh once more, which is invaluable.

Some cases are not helped at all in this way. This may often be suspected beforehand, but sometimes a fortnight's trial must be given them (Playfair), and if this is explained to them in advance, they are usually stimulated to do their best.

Perhaps the most indispensable condition for success is that the physician should gain and keep the fullest confidence of his patient. How he will best accomplish this must depend, in the end, upon his own character and temperament. If he never allows himself to be discouraged, and insists on the systematic brushing aside of morbid thoughts on the part of his patients, he will often be agreeably surprised at the results which he initiates.

James J. Putnam.
George A. Waterman.

* Milk mixed with half its bulk of oatmeal jelly answers an admirable purpose.

† The writer has found the application of the wet pack or blanket-pack for an hour or less, as recommended by Dr. Mary Putman-Jacobi ("Massage and the Wet Pack in the Treatment of Anæmia"), a useful adjunct to the massage.

NEURINE.—Neurine is a ptomaïn which is frequently found in meat and other articles of food which have undergone a certain amount of decomposition. Chemically, it is a derivative of ammonium hydroxide; is, in fact, trimethyl-vinyl-ammonium hydroxide, $N(CH_3)_3CHCH_2$-OH. It is often confused with choline; the latter, however, is trimethyl-oxyethyl-ammonium hydroxide, $N(CH_3)_3C_2H_4OHOH$. Neurine was first prepared synthetically in 1858 by Hoffmann by treating trimethylamine and ethylene bromide with silver oxide or potassium hydroxide. The name neurine is due to Liebreich,[1] who is usually credited with having obtained the substance by boiling protagon for twenty-four hours with concentrated barium hydroxide. According to later investigators, however, it seems very probable that Liebreich was dealing not with the vinyl base (neurine) but with an impure preparation of the oxyethyl base (choline).[2] More recently neurine has been obtained by Brieger[3] from putrefying horse, beef, and human flesh. Brieger also obtained it from human brains by boiling with barium hydroxide; it appears probable, however, that neurine occurs in the brain only as a result of putrefactive changes, for Gulewitsch could find no trace of it in perfectly fresh ox brains.[4] It has also been obtained from decomposing mushrooms; such mushrooms are very poisonous.

The genesis of neurine in the above cases is very obscure; it may be that it is formed from the cholin which is a part of the lecithin and protagon molecule (see articles on *Cholin* and *Lecithin*). Bayer showed that choline chloride could be transformed into neurine by chemical processes; this was done by heating the choline chloride with concentrated hydriodic acid and red phosphorus and then treating the iodine compound so formed with silver oxide. On the other hand, neurine may be converted into choline by first making the iodine compound and then heating this with silver nitrate.[5] Schmidt and Weiss,[6] moreover, found that choline and its salts could be converted into neurine by the action of micro-organisms. It is a significant fact that neurine is almost always accompanied by choline; hence it is probable that the latter is, as a rule, derived from the former by the loss of a molecule of water.[7]

Neurine is a colorless syrup soluble in water and alcohol; it has a strongly alkaline reaction and forms easily soluble salts. When heated, either dry or in concentrated solution, it decomposes with the formation of trimethylamine ($N[CH_3]_3$). With platinum chloride neurine forms a double compound $(C_5H_{12}NCl)_2$, $PtCl_4$, which is insoluble in alcohol; this compound is soluble with difficulty in hot water, from which it crystallizes in small octahedra. These crystals melt, with decomposition, at 195.5–198° C. and contain 33.6 per cent. platinum. A similar double salt is formed with gold chloride. A substance isomeric with muscarine may be obtained by treating neurine with hypochlorous acid and then decomposing the resulting compound with silver oxide.

Neurine may be isolated from organic liquids containing it by the method of Brieger. The method is essentially as follows: To an alcoholic extract of the material is added a saturated solution of mercuric chloride in alcohol. The precipitate (which contains most of the neurine) is washed with alcohol and water and then decomposed by hydrogen sulphide; the mercury sulphide is filtered off and the filtrate concentrated and taken up in alcohol.

The neurine is precipitated by an alcoholic solution of platinum chloride; the precipitate is washed on the filter with a little cold water (which dissolves the choline salt of platinum chloride) and the neurine salt is recrystallized several times from hot water.

Neurine is a very poisonous substance; 40 mgm. (injected subcutaneously) per kilogram body weight is fatal to rabbits. The symptoms are very similar to those caused by muscarine. A few milligrams of the hydrochloride injected into a frog causes within a short time complete paralysis of the extremities with, a little later, a diminution of reflex excitability. The heart is greatly slowed and finally stops in diastole, as in muscarine poisoning; atropine will cause the heart to begin beating again. As small a quantity as two milligrams is fatal for most frogs. After the administration of neurine to mammals there are profuse salivation, dyspnœa, diarrhœa (due to increased peristalsis), great slowing of the heart and a fall of blood pressure, and finally convulsions and death from failure of the respiration. Before the depression of the heart and respiration there is often a brief period of stimulation, due probably to the sensation of nausea. Cats seem to be much more sensitive to neurine than are rabbits or guinea-pigs; when a cat is poisoned with this substance there is, in addition to the symptoms noted above, a marked secretion of alkaline sweat from the ball of the foot. Many of the symptoms of neurine poisoning are antagonized by atropine, but even after the administration of this drug there remains a condition of general paralysis. The fatal dose for animals is ten times as great when the poison is given by the mouth as when injected subcutaneously.

Under the name of "neurine" a weak solution of choline was formerly occasionally used as a solvent for diphtheritic membranes.

Reid Hunt.

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NEURITIS.—Neuritis is inflammation of a nerve trunk or its branches. As a localized affection involving a single nerve it generally attacks certain nerves, such as the branches of the brachial plexus in the upper extremities, or of the lumbar or sacral plexus in the lower extremities. The cranial nerves may also be attacked by neuritis. When only one nerve trunk is affected, the condition is usually spoken of as "isolated," "localized," or "mononeuritis." When many of the peripheral nerves are involved at the same time, it is characterized as multiple neuritis, or polyneuritis, a condition meriting special description, and which will be discussed later. Neuritis may be either acute or chronic, or the symptoms of acute neuritis may persist for a long time and then become chronic.

The causes of neuritis are numerous. It may be due to traumatism such as direct wounding or contusion of the nerve, or to compression of the nerve by sudden and forcible muscular contraction; to dislocation of joints; to injury to the nerve from fragments of bone resulting from fracture; to compression of the nerve from the formation of callus; to pressure of growths; or, finally, to pressure upon the nerve trunks in the axilla during the use of crutches. Neuritis may also be caused by chemical agents such as ether, osmic acid, or alcohol, coming in direct contact with the nerve through subcutaneous injection. It may also develop from refrigeration through exposure to cold, and as a complication or sequel of various infectious diseases. It may also arise by extension from adjacent inflammation.

Patients who are addicted to the excessive use of alcohol, or those suffering from chronic toxic disorders such as gout, rheumatism, diabetes, chronic nephritis, or syphilis, are more predisposed to the development of localized neuritis after slight traumatism or exposure to cold. Arteritis obliterans and arteriosclerosis may also be considered to be predisposing causes.

Pathologically, there are various types and degrees of neuritis. We thus have: 1. Perineuritis, in which the inflammation originates in the perineurium to which it may be limited. 2. Interstitial neuritis, in which the inflammatory process is located principally in the interstitial structure of the nerve. 3. Parenchymatous neuritis, in which the nerve fibres undergo inflammation and degeneration. The first two forms represent a true inflammatory process. In the third form, the same changes often occur which usually arise as a consequence of complete division of the nerve. As these different processes vary in degree and are frequently found in combination, their clinical differentiation cannot always be accomplished.

Isolated neuritis is generally a perineuritis or interstitial neuritis. There are redness and swelling of the connective tissue enveloping the nerve, the blood-vessels of the nerve sheath are distended with blood, and there may be minute hemorrhages. Sero-fibrinous exudation and migration of leucocytes follow the hyperæmia. These changes may be limited to the sheath (perineuritis), or may extend into the substance of the nerve (interstitial neuritis). When the process is severe or of long standing, the nerve fibres may also become involved. In the parenchymatous form the inflammation begins in the nerve fibres, resulting in their degeneration and atrophy.

Symptoms.—Pain in the course and distribution of the nerve is the principal symptom. Its degree varies with the extent and intensity of the inflammatory process. The nerve trunk is sometimes swollen and extremely sensitive to pressure, the pain often radiating to the ultimate distribution of the nerve. The pain sometimes affects the entire extremity, which may become extremely hyperæsthetic. It is variously described by patients as darting, boring, burning, and occasionally shooting through the course of the nerve. It is increased by movement and is usually worse at night. Numbness and tingling may also be present. This may be attended by some constitutional disturbance as increased pulse rate and rise of temperature. Should the nerve fibres become involved, objective sensory disturbances may arise, such as varying degrees of anæsthesia in the area of the distribution of the affected nerve, with weakness or muscular paralysis. Herpetic eruption or glossy skin may also be present. In severe cases anæsthesia, paralysis, and atrophy usually take place. The faradic irritability of the nerve and muscles is at first increased, but gradually it diminishes, and is finally lost when the nerve fibres undergo degeneration.

The neuritis may ascend a nerve ("ascending neuritis"), reaching the plexus from which the nerve arises, and thus extend to several or all of the nerves of the limb. The inflammation has also been known in rare instances to extend to the spinal cord, causing subacute or chronic myelitis.

Prognosis.—Acute neuritis may disappear in a few weeks if the cause can be successfully removed. The most favorable cases are those due to slight traumatism. More commonly the affection persists in a chronic stage for many weeks or even months. The most protracted forms arise in patients with gout or rheumatism, or in such toxic cases in which the toxin cannot be removed at once. When the axis-cylinder processes are involved, as in degenerative neuritis, the condition may last for many months, paralysis and atrophy becoming permanent if the nerve fibres do not undergo regeneration. An opinion as to the prognosis often depends upon the changes in the electrical irritability of the nerves and muscles.

Treatment.—When a nerve is divided by a wound, the separated edges should at once be approximated and sutured. In compression or injuries of nerves from luxation, fracture, callus, tumors, inflammation of soft parts, abscesses, etc., it is the first duty of the physician to insist upon immediate surgical measures to free the injured nerve if possible.

A cure is not always accomplished by this method alone, inasmuch as any accompanying muscular paralysis calls for subsequent treatment. Under such circumstances surgical intervention must be the first step, otherwise all other treatment will prove futile. The general constitutional condition of the patient must not be overlooked. In acute cases absolute rest of the affected limb is essential, either by keeping the patient in bed, or by immobilization of the limb by a suitable supporting bandage. The relief of pain is an important feature. In acute traumatic cases a Chapman's ice bag applied along the course of the nerve, or cold compresses often prove valuable. The application of hot-water cloths ameliorates the pain in many cases. When anæsthetic areas are present, extreme care should be observed when hot-water cloths are applied, in order to avoid burning the skin. Blistering or superficial linear cauterization over the affected nerve trunk often effectually relieves the pain.

At times it is necessary to administer some of the coal-tar derivatives such as phenacetin, acetanilid, or salipyrin. When the pain is persistent and severe, and is not relieved by other means, we must resort to the use of opium, morphine, or codeine. Local injection of a solution of cocaine at the seat of the greatest pain often gives relief. The continuous galvanic current is also of great value in diminishing the pain. The anode should be placed over the affected nerve, the current strength being from six to eight milliampères, the application lasting five or six minutes daily. For the paralysis accompanying degenerative neuritis after the acute symptoms have subsided, the application of the labile or interrupted galvanic current to the affected muscles seems to hasten the recovery of motility by improving the nutrition of the muscles and accelerating the regeneration of the nerve. Massage is generally contraindicated during the early period of the inflammation, but it can be favorably utilized later. Small doses of mercury have been recommended by Gowers for the purpose of influencing the neuritic process.

Multiple Neuritis or Polyneuritis.—This is a disease in which many nerves are inflamed simultaneously or in rapid succession. It usually affects symmetrically the nerve trunks in the extremities, particularly in their peripheral distribution. In this form of neuritis the pathological process originates in the nerve fibres, the adventitial structures generally being involved secondarily. In mononeuritis the nerve sheaths and the connective tissue, as a rule, are primarily affected. As early as 1828 Graves described the condition as "a form of generalized paralysis probably depending upon disease of the peripheral nerves." The first authentic case with post-mortem verification was published by Dumesnil, of Rouen, in 1864, but it was not until further observations were reported by Lancereaux in 1871, Eichhorst in 1875, Joffroy in 1879, Leyden in 1880, and Grainger Stewart in 1881 that the doctrine of multiple neuritis was placed upon a sound pathological basis. During the last twenty years many observations and monographs relating to this subject have been published, the literature now being quite abundant.

Etiology.—Multiple neuritis is invariably the result of some toxic substance circulating in the blood. A very large number of different causes are active in its production.

(*a*) *Poisonous substances introduced into the system* (these being mentioned in the order of their importance): Alcohol, lead, arsenic, copper, silver, phosphorus, mercury, carbonic-oxide gas, bisulphide of carbon, and nitrobenzol.

(*b*) *Poisons originating within the body* (autotoxic): Dyscrasic conditions such as gout, diabetes, tuberculosis, carcinomatosis, syphilis.

(*c*) *As a sequel or complication of various infectious diseases:* Diphtheria, influenza, typhoid fever, smallpox, scarlet fever, measles, pneumonia, whooping-cough, epidemic cerebrospinal meningitis, erysipelas, gonorrhœa, malarial toxæmia, acute articular rheumatism, leprosy, and all forms of septicæmia.

The majority of cases of multiple neuritis are traceable to alcoholic excesses. It is hardly necessary to mention that the vulnerability of the peripheral nerves to the effect of alcohol varies in different individuals. One person may indulge in large quantities daily for years without developing neuritis, while many others who probably possess less resistance in the peripheral neurons are attacked by the disease after the continued daily use of a comparatively small amount of alcohol. The writer has seen several cases resulting from the daily use of about two ounces of whiskey continued for three or four months. Multiple neuritis as a sequel of acute alcoholic intoxication is almost unknown.

According to the preponderance of one set of symptoms over another, multiple neuritis has been classified into various clinical types, such as:

1. *A motor or paralytic type* (alcohol, arsenic, diphtheria, Landry's paralysis).
2. *A sensory type*, an ataxic form which is often described as "pseudotabes" or "neurotabes peripherica," and is most commonly due to arsenic or alcohol.
3. *A vaso-motor type* (erythromelalgia, Raynaud's disease).
4. *An endemic form* (beri-beri or kakki, particularly prevalent in Japan and the Dutch East Indies).

Multiple neuritis occurs most frequently, however, in transitional forms, and may then be characterized as a common or mixed type in which motor, sensory, and vaso-motor phenomena arise in various combinations.

Polyneuritis usually occurs between the ages of twenty-five and fifty years. Aside from the form due to diphtheria, it is rare in children, although it has been occasionally observed between two and six years of age. A number of cases of multiple neuritis in children as a result of alcoholic poisoning are now on record. In one of the writer's cases the child, who was five years old, had been given whiskey and beer daily for several months by its ignorant mother, for the purpose of strengthening it after an attack of diarrhœa. The disease rarely occurs after the sixtieth year.

Symptoms.—It is now well established that in multiple neuritis no set of symptoms is exclusively related to a single cause. A description of the symptomatology of the alcoholic form will convey a knowledge of the general features of the affection.

Multiple neuritis may be either acute or subacute in its onset, and may follow or accompany an attack of delirium tremens. The temperature may be slightly elevated in the beginning, and some fever may continue throughout the acute period of the disease. Normal temperature is not unusual. At first there is often tingling, or a sensation of "pins and needles" or numbness in the extremities, with vague sharp pains or aches, which gradually become more acute. The paræsthesiæ and pain are soon followed by muscular weakness, or paralysis, or inco-ordination. Either the upper or lower limbs or both may be involved, first and chiefly the hands or the feet. The feet are affected more frequently than the hands; motor symptoms may exist in the legs, and only sensory symptoms in the hands. This is accompanied by tenderness along the nerve trunks and in the muscles, the muscular tenderness usually increasing to an extreme degree. The co-ordinating power may be affected at the same time. Tremor is often conspicuous. Most frequently the knee jerks are absent, this depending directly on the involvement of the anterior crural nerves. The knee jerk is present or even exaggerated in some cases of slight degree, and this invariably indicates that the anterior crural nerves are intact.

In the lower extremities the nerves most commonly affected are the peronei and the posterior tibial and their branches. Occasionally the anterior crural nerves are also involved. Thus, the paralysis usually affects symmetrically the corresponding tibial group of muscles producing "foot-drop." In severe cases nearly all of the nerves of the extremities may gradually become involved, and a more or less complete paraplegia develops.

The upper extremities may escape entirely, or the paralysis is almost always of lesser degree and extent than in the lower extremities. The musculospiral nerve and its branches are most commonly affected, thus producing paralysis of the extensors of the wrist and hand and "wrist-drop." It often happens that other nerves are also involved. A peculiar feature in these cases is the implication of the nerves in their peripheral distribution, the paralysis usually being more pronounced in the distal portions of the extremity. This is also indicated by the fact that at times when the supinators and the long abductor of the thumb in the upper extremity and the tibialis anticus in the lower extremity remain intact, there may be paralysis of the other muscles which receive their supply through the same nerve trunks. Sometimes the muscles above the knees and elbows are also affected. In the more severe cases the diaphragm and the muscles of the abdomen also become involved. In rare instances several of the cranial nerves may be implicated, the facial muscles, those of the tongue, or the ocular muscles thus becoming affected. The paretic or paralyzed muscles soon become flaccid and undergo atrophy and present the reaction of degeneration. Sensory disturbances are often associated with the loss of motor power. They may be altogether absent or exist alone. In addition to the subjective sensations already mentioned, extreme hyperæsthesia may exist over the affected parts, or tactile, pain, or muscular senses may be affected in various degrees. In the ataxic form inco-ordination is the chief symptom. It is usually accompanied by muscular tenderness, and exists with or without the affection of cutaneous sensibility just described. The inco-ordination in these cases resembles closely that of tabes, hence the form in which this symptom is predominant has been called "pseudo-tabes." Its most frequent cause is alcohol, but it has also resulted from arsenical poisoning and from infectious processes.

Trophic changes occur in prolonged cases in the nails, skin, and hairs, and are similar to those of ordinary neuritis. In uncomplicated cases the sphincters of the bladder and rectum are not involved.

In some severe cases in which the neuritis is widely distributed, the pneumogastric nerve or some of its branches may become affected, causing interference with the action of the heart, the muscles of respiration, and the vocal cords.

All of the symptoms vary according to the acuteness and intensity of the disease, and they also differ according to the cause. In lead poisoning the paralysis is usually confined to the upper extremities. In alcoholism all four extremities are often affected, the arms escaping more often than the legs.

Mental Symptoms.—A somewhat characteristic disturbance of memory often takes place. In general, it may be described as a peculiar form of forgetfulness with delusions of recollection. The memory for recent events is generally confused but not always entirely lost. Occurrences of some days, weeks, or months previously are misinterpreted by the patient as of quite recent occurrence, or as having just taken place. Although he may be confined to bed and unable to move, he may assert that he has just returned from a long journey, or has been out for a ride, or has just visited friends, etc. In some cases there are insomnia, delirium, talkativeness, or incoherence, or other more pronounced manifestations of acute alcoholic insanity or confusional insanity. All of these mental symptoms are essentially due to toxæmia, and bear no direct relation to the degree or form of the neuritis. Although more commonly observed in alcoholic subjects, they are known to occur in the course of multiple neuritis due to other poisons and also from infection.

Diagnosis.—In acute cases, when all of the characteristic symptoms are present, and the patient is unable to move from the bed, the diagnosis is very simple. It is the subacute forms that often present some difficulty in their diagnosis. On account of the presence of inco-ordination, pains in the legs, and loss of knee jerks, and some objective disturbances of sensibility, it has sometimes been mistaken for tabes. It is easily differentiated from tabes, however, on account of the presence (in multiple neuritis) of tenderness of the muscles and nerves, the neural character of the pains, the symmetrical diminution or loss of muscular power, the absence of bladder symptoms, and the presence of the pupillary light reflex.

Multiple neuritis has also at times been confounded with atypical cases of poliomyelitis, but poliomyelitis is most frequent in children; its onset is abrupt, the paralysis is rarely symmetrical in its distribution, and there is generally an absence of all sensory symptoms.

The history of some form of toxæmia known to cause polyneuritis is a potent element in the differential diagnosis.

The Diagnosis of the Toxic Cause, and the Differentiation of the Various Types.—It is not always easy to determine from the clinical symptoms alone whether a certain case of multiple neuritis is caused by alcohol, arsenic, lead, or some infectious process. However, there are certain elements in the history, a peculiarity in the distribution of the paralysis, and well-defined indications associated with some special forms of toxæmia or infection, which often conclusively prove the cause of the neuritis.

For instance, the somatic and psychical symptoms may present a classical picture of chronic alcoholism. Thus, in addition to the polyneuritis, there may be tremor in the lips, tongue, and hands, toxic amblyopia, chronic morning vomiting, cirrhotic liver, albuminuria, delirium tremens, or alcoholic dementia. *Arsenical neuritis* is often accompanied by vomiting, a general brown pigmentation of the skin, and the presence of arsenic in the urine. In some cases the ataxia is more pronounced than are the motor symptoms. The arsenic has usually entered the system as a result of acute poisoning after an ineffectual attempt at suicide. Occasionally the neuritis is produced by the prolonged administration of medicinal doses of Fowler's solution as used in the treatment of chorea in children, or from the inhalation of arsenical dust given off from wall paper and other articles containing arsenic. Recently a large number of cases of arsenical polyneuritis occurred in England from the use of beer in which arsenical glucose had been used in its manufacture.*

Multiple neuritis from lead poisoning is most frequently found among those whose occupation requires frequent or continuous contact with lead. The accidental causes are numerous, such as the contamination of drinking-water by leaden pipes, the cooking of food in vessels containing lead in their manufacture, the use of various cosmetics, hair dyes, etc. It has also been traced to snuff, which was found to contain lead. As a rule, the lead enters the system through the alimentary canal as a result of uncleanliness, and the pollution of food by hands that have been in contact with lead. It may also enter the system through inhalation, and by absorption through the skin. As in other forms of toxæmia individual susceptibility to the effects of lead has much to do with the development of neuritis. People in general ill health, and those addicted to alcoholics, are more predisposed to the toxic action of lead. The upper extremities are more commonly affected, a blue line is often seen on the gums, and lead may be found in the urine (see article on *Lead Palsy*).

Polyneuritis from *diphtheria* may be attended with wasting and anæsthesia; but the weakness in the limbs usually succeeds paralysis of the palate and ciliary muscle, which are never seen in other forms of polyneuritis.

Course and Prognosis.—Multiple neuritis usually takes an acute or subacute course and reaches its height in a few weeks or a few months. It then remains stationary for about the same period, and gradually recovery takes place. Some cases are very severe and are accompanied by high fever, and may terminate fatally in a week or two from paralysis of the heart or diaphragm, or from

* Glucose is made by the action of sulphuric acid on various kinds of starch. The origin of the arsenic was found in the sulphuric acid which is commonly made from arsenical pyrites.

pulmonary œdema. It sometimes assumes a course similar to that of Landry's paralysis. The condition is always serious when the patient's general health is poor in consequence of a recent infectious disease, or in severe types of chronic alcoholism, etc. When the vagus or phrenic nerves become involved, the life of the patient may be in constant danger, although recovery has occurred even under such circumstances. When the paralysis is confined to the distal portions of the extremities, the prognosis is more favorable. In exceptional instances the course may become chronic and progressive. In the majority of cases, however, in the absence of complications the disease terminates in complete recovery. Even in favorable cases the affection may last from several months to two years or more, depending upon the underlying cause, the extent and intensity of the nerve degeneration, and the recuperative powers of the patient. The prognosis is always materially influenced by the course and virulence of the toxæmia. When the sphincter of the bladder is involved, it is usually indicative of extension of the inflammatory process to the spinal cord, thus rendering the prognosis as to recovery more doubtful.

Treatment.—The treatment of polyneuritis is essentially symptomatic. Aside from the cause of the toxæmia the various forms receive practically the same treatment. It is essential to discover, if possible, the cause of the neuritis, and to remove it or discontinue its further action. This should be the first consideration, particularly in cases due to alcohol. The sudden withdrawal of the customary stimulant is not always advisable, particularly when cardiac weakness is present. This can usually be successfully accomplished, however, by the administration of suitable heart tonics. Rest in bed, with general supporting treatment, is desirable or absolutely necessary in the majority of cases. A local or general warm wet pack for the purpose of producing diaphoresis, if the patient's strength admits, is often followed by excellent results in the early stage, or, if the patient is strong enough to bear the necessary procedures, a warm bath for fifteen or twenty minutes daily often proves beneficial. General constitutional treatment applicable to the special condition constituting the toxæmic process should never be forgotten. In order to prevent deformities, faulty positions of the extremities should be corrected by giving the necessary support to paralyzed muscles. Thus when there is "foot-drop" the feet should be kept at right angles with the leg by means of sand-bags, pillows, etc. For the purpose of relieving the pain anodynes should be administered when necessary in the same manner as mentioned in the description of the treatment of mononeuritis. When the diaphragm becomes paretic or paralyzed, artificial respiration and the hypodermatic injection of strychnine must be resorted to. Indications of heart failure are to be met by absolute rest and the administration of cardiac stimulants. When deglutition is interfered with, the patient should be fed through the œsophageal tube in order to prevent the entrance of food into the larynx or bronchi.

Fortunately such emergencies arise only in exceptionally severe cases. After all of the acute symptoms have subsided, massage and electricity will prove useful.

William M. Leszynsky.

NEURODIN, acetyl-p-oxy-phenyl-urethane, $C_2H_4.OCOCH_3.NH.COOC_2H_5$, is prepared by acetylation of the compound formed by the interaction of chlorocarbonic ether and amidophenol. It is a colorless, odorless, crystalline substance, soluble in 1,400 parts of cold water and readily in boiling water. It is antipyretic and antineuralgic in dose of 0.5–1.5 gm. (gr. viij.–xxiv.).

W. A. Bastedo.

NEUROEPITHELIOMA.—The name of neuroepithelioma was first given by Simon Flexner in 1891 to a peculiar tumor of the retina in which were found collections of cells resembling the rods and cones of the external nuclear layer. Flexner believes this tumor to have had its origin not in the supporting cells, but in the neuroepithelial cells of the external nuclear layer, and to be therefore not a glioma but a neuroepithelioma. In this tissue he found the tubular or alveolar arrangement of the cells, so common in glioma of the retina; and among the cells of the tubules he found tiny rosettes composed of long cylindrical cells, the pointed extremities of which were turned toward the lumen of the rosette and formed there a membranous ring. These cells he considered rudimentary rods and cones. He answers the objection of Iwanoff to the formation of tumors from any cells except supporting cells by quoting Klebs' opinion that all the elements of the nervous system are capable of proliferation.

Three years later, Wintersteiner reported a case of so-called neuroepithelioma of the retina in which rosettes similar to those described by Flexner were found. Wintersteiner mentions Flexner's work, but claims to have made his discovery quite independently of the latter, and does not give him credit for the name "neuroepithelioma." He found transitions between the rods and cones and the tumor cells, and considers the membrane formed by the processes of the cells to be analogous to the membrana limitans externa. In a later monograph Wintersteiner discusses eleven tumors with epithelial rosettes which he found among thirty-two gliomata, and in two cases of microphthalmos. He regards these tumors as originating in misplaced cells of the rod-and-cone layer. Several other authors have reported similar tumors, but without giving them the same interpretation. Thus Becker describes rosettes of cylindrical cells in a tumor with a marked alveolar structure which he called "tubular angiosarcoma." Bochert, Eisenlohr, Jung, Thieme, and Van Duyse probably were also dealing with the same kind of tumor under the name of glioma or gliosarcoma, or angiosarcoma. Two observers, Greef and Hertel, working with the Golgi method, were able to demonstrate the presence of true ganglion cells among the ordinary spider cells which formed the mass of the tumor in both cases. They did not, however, apply the term neuroepithelioma to these tumors, but preferred to use the name neuroglioma ganglionare, after similar tumors in the central nervous system.

The best criticism of the views of Flexner and Wintersteiner is given by Ginsberg, who examined two tumors from a case of microphthalmos, and found in them the same rosettes of epithelial cells described by the two former. Ginsberg, however, regards these as cylindrical cells from the pars ciliaris retinæ, not rods and cones. These cylindrical cells are undifferentiated cells of the original Anlage of the retina, formed before the neuroblasts and spongioblasts. As these primitive cells are of epithelial origin he suggests the name "carcinoma retinæ," instead of neuroepithelioma. He bases his theory not only on the appearance of the cells composing the rosettes, but also on the fact that these primitive, undifferentiated cells are capable of proliferation, while in the case of highly specialized cells, such as the rods and cones, there is great doubt as to the possibility of their proliferation. The tumors which Wintersteiner has called neuroepithelioma Ginsberg regards as probably formed from primitive epithelial elements, and not from the highly specialized neural epithelium.

Alice Hamilton.

NEUROFIBROMA. See *Fibroma.*

NEUROMA. See *Fibroma.*

NEUROMA OF THE SKIN, PAINFUL.—This is an exceedingly rare affection, but two cases in which the skin was primarily affected being on record. Duhring's "Case of Painful Neuroma of the Skin," *American Journal of the Medical Sciences*, October, 1873, was the first noted and was followed by Kosinski's case in the *Centralblatt für Chirurgie*, No. 16, 1874. Both cases occurred in men, aged seventy and thirty years respectively. In Duhring's case the tumors had been developing for ten years and in Kosinski's for fourteen. The tumors, varying in size from a pinhead to a filbert, confluent and disseminated, were thickly studded over the areas affected. In the first case they extended from the left scapula over the shoulder down the arm to the elbow, occupying principally the area of distribution of the circumflex nerve, and in the second case over the buttocks and upper part of the thigh, corresponding to the area supplied by the small sciatic and external cutaneous nerves. The lesions were arranged irregularly, not corresponding exactly to the course of the nerves mentioned, and formed firm, flat, or oval, elastic nodules, fixed in and extending below the skin, and movable only with it. The integument between the nodules was normal, they being purplish or pink in color. In Duhring's case the skin over the nodule was slightly scaly. At the outset pain was variable, but later it became excruciating and occurred in violent paroxysms, lasting an hour or more.

Since they are never malignant these neuromata are best not interfered with unless great distress is caused by the pain. In both the above cases resort was had to a removal of portions of the nerve supply with resulting quick relief from pain and gradual and almost complete subsidence of the nodules.

The new growth is composed of firm connective tissue and non-medullated nerve fibres.

Charles Townshend Dade.

NEUROMIMESIS. See *Joints, Chronic Diseases of.*

NEURONE, GENERAL PATHOLOGY OF THE.—Introduction.—Notwithstanding the liberal number of papers which have been published in recent years upon the pathology of nerve cells, we have still, in an essay to construct a general pathology of the neurone, only fragmentary data at our disposal. The neuropathologist, like all other special pathologists, meets with insuperable difficulties, due to the fact that a well-developed pathology of the cell in general is still lacking. Investigators are coming more and more to the opinion that in order to build up a satisfactory pathology of the cell, research ought not to be limited to the cells met with in the special tissues of highly differentiated animals, but should be extended to unicellular forms, in which the conditions of life are simpler and with which the possibilities of experiment are more manifold, and the experiments themselves are more easily subject to control. Indeed, at the present time, part of the pathology of each of the special types of cells of the vertebrate animal is based directly upon inferences drawn from work done upon one-celled species. Thanks to the very extraordinary distribution of the protoplasm of the nerve cell in space, however, it has been possible, in nerve cells or neurones, better than in any other specialized type, to study the results of injury to a part of the cell; indeed, this kind of injury can perhaps be better studied in them than in any of the simplest organisms. It is owing to this circumstance, doubtless, that such a goodly portion of that pathology of the neurone which has thus far been evolved has to deal with degenerative and regenerative processes following upon damage to some one of its parts, particularly its axone.

In view of the variety of hypotheses still advanced concerning the ultimate structure of the protoplasm of the normal nerve cell (see this Handbook, Vol. II., article, *Brain, Histology of*), it is by no means surprising that there is lack of unanimity of opinion regarding the fundamental nature of the changes which are met with in the neurone when it is diseased.

The studies of the botanist Fischer, of Leipsic, have shaken microscopical histology at its foundations. Now that we know the varying results which can be obtained, not only by the use of fixing reagents of different chemical constitution, but by the employment of the same reagent in different degrees of concentration, we must needs be chary of the conclusions we arrive at from the examination of fixation pictures in nerve cells, not only in health, but also and perhaps more particularly in disease.

The scepticism excited by these recent observations has, in some quarters, probably become excessive. Realizing that the stainable substance of Nissl can be precipitated in granules of different size by alcoholic solutions of varying strengths, that by treating nerve cells by one series of vigorous reagents, the so-called neurofibrils of Apáthy or of Bethe may be demonstrated, while by treating the same nerve cells by a different series of powerfully modifying solutions the honeycomb structure of Bütschli or the neurosome rows of Held may be put in evidence; and bearing in mind, further, that microscopic appearances similar to karyokinetic figures, centrosomes, and cytoplasmic radiations may be produced by the action of fixing reagents upon albuminous solutions injected into the empty cellular spaces of cork, there are those who would go so far as to say that the microscope and microscopical histological methods have been and can be of very little help to us in unravelling the structure and deciding upon the functions of cells. Such pessimists, however, forget the wonderful advances in neurological knowledge, anatomical and pathological, which are directly attributable to the use of the microscope. It would be as illogical for the student of the nervous system to give up the study of fixation pictures as it would be for the chemist to abandon the method of precipitation as a means of acquiring knowledge concerning the composition of solutions. It may be that the protoplasm of the nerve cell, as well as protoplasm in general, consists chiefly of colloidal particles held in suspension by virtue of the electric charges which they possess; if so, we may expect that some day new and desirable information will be derived from a study of artificially prepared colloidal solutions. Such a line of investigation, attractive and promising as it is, will unquestionably be that along which many can profitably work; but it is to be hoped that there will be others who will continue and extend those studies by histological methods which have done so much for us in the past, and which, many of us are convinced, are capable of supplying us with still more valuable information in the future.

In the brief sketch of the general pathological morphology of the nerve cell to be made here, the changes due to functional activity will first be referred to; next a description of the processes of necrosis and necrobiosis as they affect the neurone will be given, followed by a brief discussion, (1) of the various degenerations which involve the whole neurone or parts of it; (2) of regenerative phenomena; and (3) of the changes consequent upon various forms of intoxication.

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Changes due to Functional Activity in the Neurone.

In this connection the studies of Hodge upon the histology of fatigue are by far the most important hitherto undertaken. His researches were made upon the nerve cells of various animals, including sparrows, swallows, pigeons, and honeybees. A comparison of the cells of such animals captured in the morning with cells of animals of the same species killed after a long day's exercise