

digestible, a fact which has led to its examination by chemists and physicians with a view of determining its availability for use as a digestant. Its digestant principle has eluded isolation, as have all similar substances. It has been found possible, however, to concentrate the activity in a peculiar extract called caricin (Moncorvo), papain (Wurtz), or papayotin (Peckolt), which is extracted with water, the solution filtered and the filtrate precipitated with alcohol, and perhaps again dissolved and reprecipitated for somewhat further concentration. The fresh juice, which consists largely of water, yields also considerable resin, divisible into two portions, nearly five per cent. of a kind of caoutchouc, a little fat, malic acid, leucin, tyrosin, and other unimportant matters. The leaves, from which the papain can also be obtained, yield the crystalline alkaloid *carpaine* ( $C_{14}H_{23}NO_2$ ), which is most abundant in the young leaves, constituting about one-fourth of one per cent. of their weight when dried. The seeds, which are pungent and which are used for their tannicidal properties, contain a resin which shares the pungency, though the latter is said to be due to a volatile principle allied to the volatile oil of mustard.

**ACTION AND USES.**—Since about the year 1880, great attention has been given in Europe and America to attempts to employ papain as a digestant. Reports as to the energy, and even as to the manner of its action, vary most widely, even when presented by careful experimenters, and the conviction is forced that the market preparations employed by them must have differed in character. It appears very likely that some of these preparations were mixtures of different digestive ferments, the results being such as might be expected from an admixture to the papain of pancreatin or pepsin. Much of the information which has been supplied to physicians, and which has found its way into professional journals and books, has been smuggled under the guise of scientific literature from interested commercial sources.

It has been definitely established that as a digestant papaya is wholly proteolytic. It disintegrates, softens, and liquefies albumen in the form of white of egg, musculin, fibrin, and casein, and considerable of the product is peptonized. This action takes place in an alkaline or neutral medium. Davis (1893) and Hobein (1894) have shown that it is inactive in an acid medium, the papain employed by the second-named authority having been prepared by himself from papaya. Fairchild, using specimens the identity and purity of which were authenticated by himself, has fully confirmed this conclusion. Nevertheless, some eminent authorities claim that there is a slight activity in acid media. Dr. Lafayette B. Mendel, who takes this view and who has made special researches in this direction, has furnished us with the following account of the products of papain digestion:

"The products of the reaction of papain with proteids consist in large part of proteoses. Peptones—*i. e.*, compounds not precipitable with ammonium sulphate, but still giving the biuret reaction—are also formed. The papain proteoses resemble the related products obtained by gastric digestion. Regarding the occurrence of further products of proteolysis, such as leucin, tyrosin, tryptophan, and other characteristic derivatives of tryptic digestion the evidence is somewhat uncertain. Underhill and the writer have usually failed to find leucin, tyrosin, and tryptophan in appreciable quantities, at least under conditions in which they are readily formed in large quantities by other tryptic enzymes. Emmerling has succeeded in isolating small quantities of these substances from the products formed after very prolonged digestion, although even under such conditions proteoses predominate. Papain accordingly resembles trypsin in dissolving proteids in media of various reactions, thus differing from pepsin; its resemblance to the latter lies in the similarity of the products formed by the two enzymes. Harley has made comparable observations with the enzyme of the related *Carica hastifolia*. Kurajeff has found that commercial preparations of papain induce the formation of peculiar proteid precipitates

in solutions of proteoses such as the widely used 'Wittepepton.' The reaction corresponds with that described for rennin as 'plastein formation,' by Danilewski and his co-workers. The importance of this proteid-clotting or precipitating function of enzymes can only be conjectured at present. Thus it may play a rôle in proteid synthesis and regeneration; and the significance of such an enzyme in plants at once becomes apparent. On milk papain preparations exercise a clotting or curdling action. Whether these properties are all due to the same enzyme, or whether more than one unorganized ferment is present in the plant, are questions which have not yet been settled."

Riedel, who in 1894 made a very elaborate series of experiments to determine the most favorable conditions for the activity of papain, concluded that the most favorable temperature was about that of the body; that one part of papain to one hundred of albumin was the most favorable proportion; that the more concentrated the papain solution the greater the activity, and that the capacity of papain for digesting egg albumen was about one hundred times its own weight. The answer to the last question depends naturally upon the degree of concentration of the papain; yet it has been found impossible to carry this concentration more than a little way. The activity of a definite portion of the dried papaw juice itself is much greater than that of the papain extracted from it; a single instance is recorded in which such a juice, very carefully prepared, digested one thousand times its own weight. The difficulty is that this action is extremely variable; so much so that it is not at all probable that commercial dried papaw juice could ever be brought to a uniform standard of strength.

As a general statement, it may be said that a good average sample of papain is capable of digesting from fifty to one hundred times its own weight of albumen, under favorable conditions. It is also very noteworthy that it loses its power rapidly upon being kept. If kept with ordinary care in well-stoppered vials it will ordinarily have but little value at the end of a year.

As to whether papain possesses any diastasic action in the conversion of starch, we have also discordant reports, but are obliged to conclude that it has none. As to its milk-curdling power, it certainly possesses a small and variable degree; but this is of a peculiar character, the process and the coagulum differing distinctly from those resulting from the use of rennet.

Papaya is a powerful irritant to denuded tissues and to mucous membrane. So powerful is this action that if a large amount be taken into the stomach in concentrated form it acts as an irritant, or even as a caustic emetico-cathartic poison. Applied to a raw surface it acts as an escharotic, and is very apt to be followed by putrefactive processes. Papain, prepared as above described, is less active in this direction, though still irritant. Desjardins states that the irritant property is almost completely destroyed by boiling, which also produces a new substance, having a powerful lumbricidal action, similar to that of the seeds.

The principal native use of papaya has been stated above. Owing to its locally stimulant action, it has also been used as a cosmetic, to remove pimples and similar roughnesses from the skin, and to produce a smooth, healthy surface. Its irritant properties have been utilized in the form of caustic applications to cancerous and other morbid tissues, but the practice cannot be considered good. Its dissolving action upon albuminous substances has been utilized by applying it to diphtheritic membranes. For this purpose a five-per-cent. solution, preferably made alkaline with 0.5 per cent. of bicarbonate of soda or potash, is applied at short intervals with a brush, or in the form of a spray. The results appear to be highly irregular and uncertain. A similar solution, but twice as strong, is applied to warts, corns, and other cutaneous indurations. Almost its entire use in Europe and America is for internal administration as a digestant, either alone or combined with other ferments. Owing to its irritant effect it should be administered when the

stomach is full of food, and dilution with milk-sugar or other neutral substance is desirable. Opinions differ widely as to the dose, but the best evidence is in favor of the use of a considerably larger dose than that of official pepsin. Where there is an irritable condition of stomach or bowels, the dose should be reduced, and the drug should not be used in case of an ulcerated condition of those organs.

**ALLIED DRUGS.**—The juice of the fruit and leaves of the pineapple has similar properties and uses, already referred to under *Bromeliacea*.  
*Henry H. Rusby.*

**PARA-ACET-AMIDO-PHENOL ETHYL CARBONATE**, a tasteless, white, crystalline powder, insoluble in water and readily soluble in alcohol, is administered in dosage of 0.5 gm. (gr. viij.) as an antipyretic, analgesic, and hypnotic.  
*W. A. Bastedo.*

**PARA-CHLORALOSE.** See *Chloralose*.

**PARACHOLIA.**—The term used by Pick to designate the hypothetical secretion-anomaly by which the bile leaves its accustomed channels and passes into the blood, giving rise to icterus. By a number of recent writers icterus is regarded as due to a diseased condition of the liver cells, the process being analogous to the secretion of albumin in diseased conditions of the kidney cells. Normal liver cells should secrete bile into the bile vessels, and urea and sugar into the blood capillaries. According to Minkowski it is, therefore, not without analogy that the liver cells in diseased conditions should give off the bile into the blood-vessels. Such a process is designated by him as *parapedesis*. Liebermeister and Pick also explain many forms of icterus as due to functional disturbances of the liver cells, either with or without evident anatomical changes, the former designating such a disturbance as *diffusion* or *akathetic icterus*, the latter as *paracholia*. Pick believes that the pathogenesis of the obscure forms of icterus may be explained by this hypothesis. He accordingly distinguishes three classes: *nervous paracholia*, *toxic paracholia*, and *infectious paracholia* (*Wiener klin. Wochen.*, 1894).  
*Aldred Scott Warthin.*

**PARADISE SPRING.**—Cumberland County, Maine. POST-OFFICE.—Brunswick. Hotels and inns.

This spring is located about one mile from the centre of the village of Brunswick and five hundred feet from the Androscoggin River. It is reached by way of the Maine Central Railroad to Brunswick, and thence by Jordan Avenue. The country about the place is level—a sandy plain, covered by pines extending to beautiful Casco Bay, three miles distant. Concerning the meteorological conditions prevailing about Brunswick, we are indebted to Prof. Leslie A. Lee, of Bowdoin College, for the following description: "The climate of Brunswick is peculiarly agreeable. Fair weather predominates, the annual number of cloudy days averaging not more than eighty-six in a long period of years. The prevailing winds are from the southwest during the summer and from the northwest during the winter. On this account the air is much drier than would be expected from the proximity of the village to the sea, and fogs rarely occur."

Scattered throughout the town are large areas of pine forests, which give a resinous and balmy quality to the air. The average annual temperature is 44.40° F., rising to an average of 65.11° F. in the summer, and falling to a mean of 22.63° F. in the winter. The temperature of the spring water is about 45° in summer and 43° F. in winter. The outflow of water is abundant, being estimated at twelve thousand gallons per day. The following analysis was made by Prof. Henry Carmichael, of Bowdoin College: Reaction neutral. One United States gallon contains: Silica, gr. 0.38; iron oxide, a marked trace; calcium sulphate, gr. 0.06; calcium carbonate, gr. 0.07; magnesium carbonate, gr. 0.06; sodium chloride, gr. 0.02; sodium carbonate, gr. 0.36; potassium chloride, gr. 0.04. Total, 0.99 grain.

A more recent analysis by State Assayer Franklin C.

Robinson shows a somewhat larger proportion of solids, viz., 1.05 grains per United States gallon of inorganic salts. The water is remarkably free from organic matter, containing, according to Robinson's analysis, but 0.07 of a grain per United States gallon. This organic matter was found by examination to be of vegetable origin, only a minute trace of nitrogenous material being detected. The water is excellent for table use, and has been supplied to the students of Bowdoin College for some time past. It is used commercially.  
*James K. Crook.*

**PARAFFIN INJECTIONS.** See *Reparative Surgery*.

**PARAFFIN-XYLLOL** is a solution of 1 gm. of paraffin in 10 c.c. of xylol, and is used as an antiseptic varnish for the hands in surgical operations.  
*W. A. Bastedo.*

**PARAFORM**—paraformaldehyde, triformal, trioxymethylene ( $HCOH$ )<sub>3</sub>—is a polymer of formaldehyde occurring as a white, insoluble, crystalline powder. It tends to decompose slowly with the production of formaldehyde gas, and, when acted upon by heat, as in some of the formaldehyde generators, may evolve the gas rapidly and in large quantities. On account of its slow and steady evolution of formaldehyde, it is used by physicians as an intestinal antiseptic and by dentists for disinfecting cavities. The dose is 0.5–1 gm. (gr. viij.–xv.). Unna prescribes: R Paraform 2 gm. (gr. xxx.), ether 2 c.c. (℥.xxx.), and flexible collodion 15 c.c. (ʒ. ss.) as the best application for pityriasis versicolor, erythrasma, and other saprophytic skin diseases. Mense uses a three-per-cent. paraform collodion as a slow caustic for warts and other small cutaneous growths.

Paraform enters into the composition of eka-iodoform.  
*W. A. Bastedo.*

**PARAISO HOT SPRINGS.**—Monterey County, California. POST-OFFICE.—Paraiso Springs. New Cottages. ACCESS.—Take 8:15 A.M. Southern Pacific train from the corner of Third and Townsend streets, San Francisco, reaching Soledad station at 1:43 P.M. Thence by stage a drive of one hour and a half to the springs.

"Paraiso Springs," says Mr. E. S. Harrison in his history of Monterey County, "were the property of the Mission Soledad, which lies about five miles northeast of the springs. The title of the present owner was obtained from the Church of Rome, to which a patent was granted by the Mexican Government in 1778. In the records of the Mission Soledad the healing and invigorating qualities of these waters are duly set forth. The springs are situated in a picturesque alcove of the Santa Lucia Mountains on the western border of the Salinas Valley, about one hundred and fifty miles south of San Francisco. The altitude of the location, being nearly one thousand feet above the valley, renders the atmosphere dry, bracing, and invigorating. Below the resort, and for miles beyond, the eye scans the fertile valley, traversed by the grand Salinas River and Arroyo Seco, and the far-away Gabilan Mountains, forming a picture of great charm and glory. The commodious hotel and cottages combine all the luxury and comforts that can be found anywhere. On the premises are several valuable springs flowing about two thousand gallons of water per hour, and consisting of sulphur, soda, and iron waters. The temperature of the springs varies from 100° to 118° F. We give below the analyses of the waters of the two principal springs, the Paraiso Sulphur Spring and the Great Paraiso Hot Soda Spring.

*The Paraiso Sulphur Spring.*—According to the analysis made by Dr. Anderson in 1889, one United States gallon contains: Sodium chloride, gr. 2.76; sodium carbonate, gr. 1.15; sodium sulphate, gr. 37.10; potassium sulphate, gr. 0.83; magnesium carbonate, gr. 6.09; magnesium sulphate, gr. 2.19; calcium carbonate, gr. 0.89; calcium sulphate, gr. 4.40; ferrous oxide, gr. 0.73; silica, gr. 2.55; organic matter, gr. 7.85. Total, 66.04 grains. Gases: carbonic-acid gas, 2.04 cubic inches;

sulphureted hydrogen, 9.25 cubic inches. Temperature, 114° F.

This is said to be one of the best bathing waters on the coast.

*The Great Paraiso Hot Soda Spring.*—One United States gallon contains: Sodium chloride, gr. 3.37; sodium carbonate, gr. 5.06; sodium sulphate, gr. 34.60; potassium chloride, gr. 0.32; potassium sulphate, a trace; magnesium carbonate, gr. 0.75; magnesium sulphate, gr. 1.10; calcium carbonate, gr. 1.30; calcium sulphate, gr. 6.45; ferrous carbonate, gr. 0.89; alumina, gr. 0.56; silica, gr. 2.90; organic matter, gr. 4.15. Total, 61.45 grains. Free carbonic-acid gas, 2.95 cubic inches. Temperature of water, 118° F.

Qualitatively this water closely resembles the famous Carlsbad Sprudel water, but is less highly mineralized. Thousands of visitors, invalids, and pleasure-seekers visit Paraiso Springs yearly, and the excellence of the mineral waters, the salubrity of the climate, and the picturesqueness of the location bid fair to make Paraiso one of the most prominent health resorts in California.

James K. Crook.

PARAKERATOSIS. See *Cornification*.

**PARALDEHYDE.**—Parethylaldehyde:  $3(C_2H_4O) = C_6H_{12}O_3$ . Paraldehyde is a polymeride of common ethylic aldehyde, producible by the action of a considerable number of substances upon such aldehyde. Paraldehyde is, at ordinary temperatures, a liquid, colorless, of a burning taste and powerful and penetrating ethereal odor. It dissolves in 8.5 parts of cold water and in 16.5 parts of boiling water. It mixes in all proportions with alcohol, ether, and fixed or volatile oils. At 0° C. (32° F.) paraldehyde solidifies to an ice-like crystalline mass, or may crystallize in distinct prisms. It should be kept in well-stoppered, dark amber-colored bottles, in a cool place. Paraldehyde is peculiar among ethereal bodies for possession of the property of determining sleep, with a minimum of by-effects. The sleep produced by the medicine seems a quite perfect imitation of natural slumber, since the subject under the influence of the hypnotic is as easily awakened as from ordinary sleep. No worse derangements occur from the medicine than a little dryness of the throat and thirst, and a trifling reduction of pulse rate and arterial tension. The most disagreeable circumstance attending the use of paraldehyde is a persistence of the taste of the drug upon the palate, and of the odor in the breath, often for a number of hours after the taking. Also it may disorder the stomach. The sleep produced by a perfectly legitimate dose of paraldehyde may begin within fifteen minutes after the swallowing, and last five, six, or seven hours. The medicine is used exclusively for the procurement of sleep, and is applicable, without special contraindication, for any case in which that therapeutics is proper. A quantity of from 2 to 4 gm. (from  $\mathfrak{m}$  xxx. to lx.) is the average dose, and the same is best given dissolved in 30 gm. (fl.  $\mathfrak{z}$  i.) of an aromatic water, sweetened.

Edward Curtis.

**PARALYSIS.**—The term paralysis, in its more limited sense, denotes complete or very pronounced loss of muscular power. The term paresis is sometimes employed to designate lesser degrees of loss of power. Paralysis is the result of functional or organic changes in the nervous system (central or peripheral), but in a comparatively rare group of diseases it is due to primary changes in the muscular fibres (pseudohypertrophic paralysis and allied forms).

Loss of muscular power may vary widely in its distribution. When confined to a single limb or part of a limb, it is known as monoplegia; when it involves one side of the body it is called hemiplegia. If the hemiplegia is present on both sides of the body, the term diplegia is used. Paraplegia is paralysis of both lower limbs (usual form), of both upper limbs, or of all the limbs.

In ascertaining the existence of paralysis of any part of the body, we must not be satisfied with merely noting

the absence or diminution of motion in the suspected part. We must also make sure that there is no mechanical obstruction to motion, such as ankylosis, fracture or dislocation, and that it is not inhibited by pain. Furthermore, the patient must be in a condition to understand our directions. Even when the patient is profoundly comatose, we may usually diagnose the existence of paralysis by noting the increased resolution and flaccidity of the parts when compared with the corresponding ones on the opposite side of the body.

Various instruments, called dynamometers, have been devised to test the amount of muscular power, but they are unnecessary for practical purposes and for the most part unreliable. If the paralysis is very marked, the loss of function is forthwith noticeable. If the loss of power is not so pronounced, the patient is directed to overcome the resistance to various movements offered by the physician. For example, in order to test the power of the quadriceps femoris the patient is directed to flex the thigh on the abdomen, against the resistance offered by the physician. This is then compared with the resistance offered on the healthy side (it must not be forgotten that the right limbs are usually somewhat stronger than the left). In cases of paraplegia we must rely upon our knowledge of the degree of resistance which should be offered normally, taking into consideration the muscular build and habitus of the patient, his general nutrition, intelligence, etc.

We must always be on our guard against mistaking paralysis for the immobility due to painful affections. For example, a case of acute articular rheumatism in a child was sent to us with the diagnosis of paraplegia, the apparent paralysis being due merely to the pain in the joints.

We must next determine whether the paralysis is functional or organic. Functional paralysis is usually hysterical and the general condition of the patient exhibits the evidences of that neurosis. Hysterical paralysis rarely affects individual nerves. It generally involves muscles in functional groups, not according to strict anatomical distribution. Some symptoms are usually found which point directly to a non-organic origin. For example, in the recumbent posture the paralyzed legs may be capable of certain voluntary movements, or they may be moved involuntarily during excitement, while on attempting to walk the loss of power may appear absolute. Furthermore, hysterical paralysis is often preceded by undoubted hysterical seizures, and it may change very rapidly in degree. Sensory disorders are very common and, like the loss of motion, are not confined strictly to the anatomical distribution of individual nerves. They consist very often of hemianesthesia, accompanied by concentric narrowing of both fields of vision.

The differentiation of peripheral from central paralyses is usually not a difficult matter. The muscles affected in the peripheral forms are supplied by one or more nerves, and a knowledge of the functions of the muscles will enable us to recognize these nerves. As the majority of the motor nerves are mixed in character, the distribution of the attendant sensory disturbances will aid still further in localizing the lesion. In mild cases there may be no change in the electrical reactions of the muscles; in severer cases there may be all possible gradations between simple diminution of electrical irritability and complete degeneration reaction. The latter is also observed, however, in certain forms of spinal-cord disease.

Atrophy of the muscles is common in peripheral paralysis, but extremely rare in cerebral paralyses; it is a constant symptom of diseases of the anterior horns of the spinal cord.

Paralysis of spinal origin usually takes the form of paraplegia, and is attended not infrequently by interference with micturition, defecation, and the sexual function. The limbs may or may not undergo atrophy, and they exhibit the degeneration reaction, according as the anterior horns are implicated or not. The patella reflexes may be lost, but if the lesion is situated high up in the cord, the tendon reflexes as well as the cutaneous reflexes may

be greatly exaggerated. Contractures are apt to develop, and are perhaps more pronounced than in any other forms of disease.

Cerebral paralysis is usually hemiplegic in character, and its onset is generally attended by symptoms of apoplexy; sensory symptoms are subsidiary. Hemianesthesia is sometimes present at the beginning of the seizure, but usually disappears in a few days. The paralyzed muscles rarely undergo atrophy and the electrical reactions are unchanged. Contracture of the muscles develops after a while and, like the paralysis, is more marked in the upper limb.

In the majority of cases the diagnostic features described above will enable us to locate the lesion which has produced the paralysis, but in exceptional cases a probable diagnosis alone can be made, after giving due weight to the attendant symptoms, etiology, etc.

The prognosis and treatment of paralysis will depend upon the primary disease, and will be considered in the various special articles.

Leopold Putzel.

**PARALYSIS AGITANS.**—(Synonyms: Shaking palsy, Parkinson's disease.)

**ETIOLOGY.**—Paralysis agitans is one of the diseases of advancing years, and the large majority of cases develop after the age of forty to forty-five years. It is a mistaken idea, however, to regard it as an indication of senility. In a few exceptional instances the disease has begun at a much earlier period, and cases have been reported at the age of twenty, seventeen, twelve, and even three years. It is very often difficult to determine the exact period at which it begins, because the inception is usually very gradual and is often unnoticed by the patient.

Unlike other neuroses, heredity plays a very slight part in this affection. Only a few cases have been reported in which other members of the patient's family suffered from this or some other form of nervous disease.

Paralysis agitans is a rare disease. Among 4,600 patients under my observation, during a period of eleven years, at the Clinic for Nervous Diseases in the Bellevue Outdoor Department, there were 30 examples of paralysis agitans, 19 of which occurred in males, 11 in females.

It has been said that the Anglo-Saxon race is especially predisposed to the disease. At all events there can be no doubt that reports of cases are comparatively rare in the otherwise very prolific German literature on nervous affections. We may also state, with regard to New York, that the disease is frequently mistaken here for senile tremor or multiple cerebrospinal sclerosis.

Prominent among the exciting causes stands emotional excitement, usually of a depressing nature, such as fright and anger. Several cases of this kind were observed among the inhabitants of Metz and Strasburg during the sieges experienced in the Franco-Prussian war. Lorain (*Arch. de Méd.*, vol. i, 1875, p. 214) reports the following striking example: A girl, aged seventeen, was frightened by the bursting of a shell in the cellar in which she had taken refuge during the siege of Paris. This was followed immediately by tremor of the right arm, which soon extended to the rest of the body. At the end of five years she was still suffering from paralysis agitans.

Long-continued worry and grief appear to act in the same way as sudden emotions.

Living in damp rooms, or protracted exposure to wet and cold, is also said to give rise to the disease, and in our experience this has seemed to be the most efficient of all the etiological factors. Some patients inform us that the tremor began immediately or shortly after catching cold, from a single exposure to wet or cold, but it is doubtful whether there is any real connection between the two events.

A number of cases have been reported in which the disease had a local origin in an injury to the arm or leg (sometimes, perhaps, as the result of a peripheral neuritis). In such cases the tremor begins usually in the injured part, but then spreads to the rest of the body and pursues the ordinary course of paralysis agitans.

Ball claims that paralysis agitans and insanity are associated more frequently than is commonly believed. The insanity, according to this writer, is always of a depressive character, generally melancholia, with suicidal impulses and numerous hallucinations. In some cases a condition of dementia and of "demi-stupor" predominates.

**CLINICAL HISTORY.**—When the disease begins slowly, as usually happens, it is sometimes preceded by prodromes. These consist of wandering pains in different



FIG. 3737.—Position of the Body in Paralysis Agitans. (From Seifert: "Diagnostik u. Therapie d. Nervenkrankheiten.")

parts of the body, occasional formication, or a feeling of weakness in the parts that are attacked at a later period by the tremor. In some instances the tremor does not remain constant after its first appearance, but subsides at times until again provoked by some exciting cause. In rare cases the disease begins suddenly, as we have seen in the section on etiology, and may spread quite rapidly to the entire body.

In the majority of cases tremor first appears in an arm or leg (usually the former), and then extends to the other limb on the same side. After a longer or shorter time (sometimes several years) it spreads to the other side of the body, generally attacking the latter in the same order. The head and trunk may also become involved. Charcot claimed that the apparent tremor of the head was always the result of the transmission of the movements of the trunk and limbs. This has been disproven by numerous cases, and several instances have fallen under our own observation. In rare cases the tremor first attacks the arm of one side and the leg of the opposite side, or it assumes a paraplegic form, involving both lower limbs. But sooner or later it extends to the rest of the body.

Coincidentally with the tremor (in some cases even preceding it) the muscles of the body acquire a certain degree of rigidity, and the body assumes a peculiar, almost pathognomonic, position, as shown in Fig. 3737.

The motor power of the limbs remains comparatively unchanged for a long time, even for many years, but in the last stages general paralysis sets in. Sensation is unaffected throughout the entire course of the disease. The

reflexes are unchanged. Unless life is terminated by some intercurrent disease, the patient finally lapses into a condition of mental hebetude, becomes bedridden, and loses power over his limbs; then the functions of the bladder become impaired, bedsores develop, and finally death ensues.

We will now enter into a more detailed examination of the various symptoms.

The tremor, which is one of the most striking features of the disease, and the one from which, in fact, it derives its name, consists of very quick, uniform, and limited excursions of the affected parts during repose. There are usually four or five oscillations in a second. In the first stages the patient is able to control the tremor for a time by an effort of the will, or by executing a voluntary movement of the parts. But, as the disease advances, this power is diminished, and, finally, while the patient may, for a very brief interval, moderate the severity of the tremor, a voluntary effort is soon followed by increased violence of the movements. The tremor subsides during sleep, but the patients are very restless at night and do not remain long in one position. The cessation on voluntary effort was regarded by Charcot as a pathognomonic differential sign, distinguishing the disease from the tremor of multiple sclerosis. But Westphal has reported a case in which the tremor of sclerosis presented the same characteristics as that of paralysis agitans; and a similar case, in which an autopsy was obtained, has come under my own observation. Magnan has also reported a case of paralysis agitans, in which the movements did not occur unless the patient performed some voluntary act which required a certain degree of attention on his part. As a rule, the fingers and forearm are the parts most affected; next follow the foot and leg. In the large majority of cases the head also presents rhythmical movements, but these are generally conveyed from the trunk and limbs. In not a few cases, however, certain of the facial muscles, particularly of the lips and chin, present tremulous movements similar to those of other parts. In still rarer cases the tongue, when protruded, also presents oscillatory movements, but these are never so pronounced as in other muscles.

Rosenberg has reported a rare case of tremor of the velum palati and epiglottis. The laryngoscope showed that the vocal cords came together promptly on phonation, but the tension of their edges changed, the gap between them being sometimes linear, sometimes a broad ellipse. The body of the vocal cords showed twitching movements, which had the same rapidity as the general tremor. When the patient was directed to hold a note as long as possible, a rhythmical change from high to low pitch became noticeable.

The appearance of the body, when the disease is fully developed, is highly characteristic, and, indeed, almost pathognomonic.

The face has a peculiarly stolid, rigid appearance. The eyes have a dull, lack-lustre look, and their movements are slow, as if the muscles were rigid like those of the face and rest of the body. Two cases have been reported in which so-called ocular lateropulsion was observed. The patients, while reading, experienced a certain amount of difficulty in directing the gaze from the end of one line to the beginning of the next line. This is most noticeable if the reading matter is arranged in columns. When they have arrived at the end of a line, the eyes involuntarily seek the corresponding line in the next column, because the ocular muscles cannot be moved with the normal rapidity.

The facial muscles have lost their emotional play almost entirely, and the face therefore looks as if covered with a mask. At times the muscles of the mouth and chin present tremulous movements similar to those observed in the extremities. The mouth is sometimes kept slightly open, and the saliva may dribble constantly in advanced cases. Speech is slow, labored, and extremely monotonous. It sounds as if the muscles of speech had to overcome some unusual resistance before the words can be enunciated. The speech is unchanged by emo-

tional excitement, and, if we may use the expression, appears to be covered by a veil. According to Buzzard, the piping voice of old age is really a symptom of paralysis agitans, and not of senility. In certain cases the words sound as if they were jolted out of the patient's mouth, like the conversation of an unskilful rider while on horseback.

The head is held forward, and the chin may even be closely approximated to the sternum. The muscles of the neck are usually rigid and offer considerable resistance to passive motion. Three cases, I believe, have been reported in which the head was drawn backward instead of forward. A fourth one has come under my observation. In some cases the muscles of the neck present independent tremor, but their movements are usually conveyed from the trunk. In the latter event the head will remain quiet if the movements of the body are forcibly restrained. The trunk is generally in a condition of anteroflexion, as shown in Fig. 8787. The arms are usually drawn slightly forward, and the elbows are slightly separated from the side of the chest. The forearms are strongly flexed, partly pronated, and they ordinarily lie across the abdomen. These parts are in a state of constant tremor, though this is not so vigorous as in the hands. The fingers are usually flexed, the thumb is adducted, and also very slightly flexed. The thumb and index finger are continually moving to and from one another, as in the act of writing, or making pills; the other fingers are in a condition of constant fine tremor. In other cases the position of the fingers resembles that of arthritis deformans, but the joints are not swollen as in the latter disease.

The lower limbs are moderately flexed at the thighs and knees, and the latter are drawn inward. The feet are in the position of equino-varus. The toes are extended at the first phalangeal joint and flexed at the other phalangeal joints.

The patient's gait is also very characteristic. Upon attempting to rise from a chair a certain amount of difficulty is experienced, as if he were compelled to overcome some resistance. He stands still for a moment, as if to steady himself, and then makes short, shuffling steps. The gait gradually increases in rapidity, and may soon pass into a sort of slow dog-trot. In many cases the patient loses his balance and falls, unless supported. Others measure with the eye the distance between the starting-point and their objective point, and learn to regulate their muscular effort in such a way as barely to reach their destination in safety. This so-called festinating gait has been attributed by most writers to the forward displacement of the centre of gravity of the body, so that the body is, as it were, hurried along in order to catch the centre of gravity. This explanation is insufficient, as is shown by the phenomena of propulsion and retropulsion. In some cases, if, while the patient is standing still, slight traction in a forward direction is exercised upon his clothes, he will be irresistibly impelled to move forward in the peculiar manner described above (propulsion). In rare cases, if the traction is exercised backward, the patient will move in this direction in a similar manner (retropulsion). In still rarer cases, the patient exhibits a tendency to move to the side (lateropulsion). In retropulsion, indeed, he is moving in a direction opposite to that of the action of the centre of gravity. Retropulsion and propulsion have also been regarded as forced movements, like those produced by irritation of the cerebral peduncles.

The muscular power of the patient is not much diminished until he becomes bedridden, but he is very easily tired by muscular exertion. Furthermore, an unusually long time elapses before the patient is able to execute any voluntary movement, and when this has been begun it cannot be discontinued as abruptly as in health. This may be readily detected by directing the patient to squeeze one hand firmly and rapidly, and comparing this action with that of a healthy individual. Although the difference is often quite decided, the dynamometer may fail to reveal any real loss of power.

Many patients suffer constantly from a feeling of heat in the skin, or from sudden flashes of heat. In addition, they complain of an indefinable internal restlessness which impels them to change position very frequently. This is often very distressing at night, since many of the patients are unable to turn voluntarily from side to side on account of the rigidity of the muscles of the trunk.

The cutaneous and tendon reflexes and sensation are unaffected, but in a few cases increase of the knee-jerk has been reported. The sufferer may complain occasionally of pains in the limbs, but the pains are felt chiefly in the back. As the disease advances, the muscular power of the patient is gradually impaired, and finally he is compelled to remain in bed. Then bedsores may develop, the sphincters of the bladder and rectum become paralyzed, and the patient dies of exhaustion. In these cases the mental powers are also apt to undergo very marked deterioration.

Probably in the majority of cases, however, death is the result of intercurrent diseases, among which pneumonia seems to play an important part.

In rare cases paralysis agitans runs its course without tremor. Such patients present all the other evidences of the disease—muscular rigidity, characteristic position of the body, festinating gait, speech disturbances, the sensation of superficial heat, etc.—but the tremor is entirely absent, or is observed only at times to a mild degree.

Within the last few years a few autopsies have been made with the aid of the most approved methods of examination. Kelscher found that the ganglion cells of the cord were strongly pigmented, with granular degeneration in places; degeneration of the nerve fibres, particularly in the posterior columns and in the peripheral nerves; in places the muscular fibres exhibited atrophy and fatty or hyaline degeneration. The interstitial tissue in the cord, the peripheral nerves, and the muscles was increased; the glia of the spinal cord, especially in the cortical layer and around the vessels, was thickened, particularly in the posterior and lateral columns. The walls of the vessels showed thickening, in places miliary aneurisms and hemorrhages.

Sander found, in addition to glia proliferation in the white substance, a similar condition in the gray matter throughout the cord; this was most pronounced in the anterior horns and in Clarke's columns. There were marked arteriosclerotic changes in the finest vessels, with periarteritic and endarteritic processes. In the parts most severely affected there was distinct degeneration of the medullary sheaths of the nerve fibres.

Dana found connective-tissue proliferation in the region of the oculomotor nucleus, very marked atrophy of the cells of the nuclei of the ninth, tenth, and eleventh nerves, and slight atrophy in the facial nucleus; also thickening of the spinal pia mater, dilatation and thickening of the walls of the vessels, especially in the anterior horns of the cord, with atrophic changes in the ganglion cells.

It is very probable that all of the changes found in these autopsies are non-specific in character. They are similar to the senile changes which are commonly found in the central nervous system, and which have also been observed in chronic alcoholism.

Nor must it be forgotten that not a few carefully observed cases have shown entirely negative findings. Hence the disease must still be regarded as a functional neurosis.

DIAGNOSIS.—When the disease is fully developed the diagnosis is extremely easy. But in its early stages it may be mistaken for multiple cerebrospinal sclerosis, senile tremor, or toxic tremor, especially after mercurial poisoning.

Multiple sclerosis is distinguished by the following symptoms: The tremor is coarser and not so rhythmical as that of paralysis agitans, and, with the exception of very rare cases, it occurs only during the performance of voluntary movements. The characteristic position of

the body and the peculiar appearance of the face are wanting, while nystagmus, diplopia, and various other cerebral symptoms of serious import are present.

Senile tremor may be as uniform and fine as that of paralysis agitans, but it generally begins in the muscles of the head and neck, and is uninfluenced by repose or motion. The head may be bent forward, but rather as the result of bowing of the back. The patient does not suffer from the peculiar restlessness of paralysis agitans, and the muscular rigidity incident to the latter is wanting. There are also other evidences of senility in the general condition.

In mercurial tremor, examination will always show that the affection has been preceded by the buccal symptoms of mercurial poisoning. The disease is also attended by greater impairment of muscular power and general prostration. The tremor is much more marked during action than during repose. In severe cases it is said to be attended at times with profound deterioration of the mental faculties. This affection appears to be extremely rare in New York, and the very few cases which have come under my observation have occurred in looking-glass makers.

Post-hemiplegic chorea sometimes appears as a fine muscular tremor, and at first sight may be mistaken for paralysis agitans, especially in view of the fact that there is considerable restoration of muscular power in the paralyzed side before the tremor begins. In addition, there is always rigidity of the affected parts. But the clinical history shows that the disease began with an apoplectic attack, and, in addition, the tendon reflexes are always exaggerated. Finally, the subjective symptoms of paralysis agitans are wanting.

PROGNOSIS.—No authentic case of recovery from this disease has been heretofore reported. Indeed, recovery might be looked upon as convincing proof of an error in diagnosis.

During the first stages of the disease temporary remissions sometimes occur, but after a time it shows slow but uninterrupted progress.

The patients usually die of an intercurrent disease, and in many cases life does not appear to be shortened by the malady. Cases have been reported in which it continued for more than thirty years.

TREATMENT.—The most that can be hoped for from treatment is to produce a certain degree of palliation of the symptoms. In our own hands slight benefit has been derived, in a few cases, from the use of galvanism, nitrate of silver, hyoscyamine, and prolonged rest in bed. Electricity has been employed by me in the form of the constant current of moderate strength, one electrode being placed on the upper cervical spine, the other on the lower dorsal region; sittings three times a week, each one of from five to ten minutes' duration. This plan of treatment must be continued for a long time in order to produce any good results whatever. Nitrate of silver may be given in pill form for a year or more consecutively, but it is well to intermit its administration from time to time. The dose may vary from gr.  $\frac{1}{4}$  to gr.  $\frac{1}{2}$  t.i.d.

Hyoscyamine sometimes produces very rapid and brilliant temporary results in diminishing the tremor. Even when the tremor is very violent and widespread, it may subside almost completely in a few days. The initial dose should not exceed gr.  $\frac{1}{100}$ , but this may be gradually increased until the physiological effects are produced. But unfortunately the good effects of this remedy cease as soon as it is discontinued, and it does not seem to us to be entirely safe to give it continuously in sufficient doses for any length of time.

Absolute rest in bed may also exert a favorable influence, but it is very difficult, on account of the great restlessness of the patient, to secure his consent to prolonged treatment in this way. Suspension has been employed in treatment, but its effects appear to be very fleeting, and in some cases it produced harmful results. In the majority of cases we are finally compelled to resort to morphine in order to relieve, in a measure, the sufferings of the patient.

Leopold Putzel.