Critical Digest.

MYASTHENIA GRAVIS.

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THE disease known as myasthenia gravis has hitherto attracted little attention in this country. Nevertheless some sixty cases have been recorded within the last few years, chiefly by German writers, and the disease has found a recognised place in German text-books on neurology.

We have ourselves had the opportunity of examining nine cases.

The disease has received various names. The earlier cases were published as "cases of bulbar paralysis without discoverable anatomical changes," and some recent writers have adopted this nomenclature. Strümpell introduced the term "Asthenic bulbar palsy." The affection is, however, not confined to the bulbar muscles. Other names which have been employed are "general profound myasthenia," "Erb's disease," the "Erb-Goldflam" and the "Hoppe-Goldflam-symptom-complex." Jolly has proposed the term "myasthenia gravis pseudo-paralytica," and this, or for short "myasthenia gravis," appears to us the most suitable and convenient hitherto suggested.

SALIENT FEATURES OF THE DISEASE.

There is weakness, sometimes amounting to complete paralysis, of some or all of the voluntary muscles. After prolonged rest of the affected muscles, *e.g.*, the first thing in the morning, they may respond normally to the will, but

they become rapidly exhausted after voluntary contractions, regaining their power again after rest. In severe cases, however, weakness and, indeed, actual paralysis may persist even after prolonged rest.

The affected muscles often exhibit the "myasthenic reaction," becoming exhausted by faradic stimulation just as they are by voluntary effort; galvanism, on the other hand, having little power in this respect.

The entire system of voluntary muscles may be affected, but those muscles are most apt to be implicated which normally act most constantly, such as the cervical muscles and the extrinsic muscles of the eye-balls. The bulbar muscles are very generally involved. Hence the term "asthenic bulbar paralysis."

A characteristic feature of the disease is its tendency to fluctuate in severity from day to day, or from week to week, or even to disappear for months or years, to reappear.

There are no sensory symptoms. Death occurs in a large proportion of the cases, but no structural changes have been discovered to account for the symptoms.

Historical.

Wilks (1), in a paper published in *Guy's Hospital Reports* for 1877, describes a case of bulbar paralysis in which no anatomical changes were found after death. This is the first reference to myasthenia gravis to be found in the literature.

Erb (2), in the following year, described a peculiar form of bulbar disease ("einen eigenartigen wahrscheinlich bulbären symptomen complex"), the characteristic symptoms of which were: ptosis, weakness of the jaws and neck muscles; and of secondary importance—weakness of the tongue and extremities, difficulty in swallowing, and weakness of the upper part of the face.

The publications of Wilks and Erb do not appear to have attracted much attention, for no further publication followed until 1887, when two cases were recorded, the one by Oppenheim (5), the other by Eisenlohr (4). In 1890 two cases were described by Bernhardt (7) and Leonard Shaw

(6), but it was not until the papers of Jolly (8), Hoppe (11), and Goldflam (9) appeared, that the disease was established as a definite clinical entity.

Hoppe, in 1892, was the first writer to give a full account of the disorder.

In 1895 Strümpell* reviewed the literature of the disease and collected twenty undoubted examples which had been reported up to that time. In 1898 an excellent *resumé* of the subject appeared by Laquer (40) of Frankfort.

During the last four or five years there have been numerous additions to the literature of the disease, and there are now some sixty or seventy cases on record, ten having been described in this country. †

The most complete account of the disease published in this country is that of Buzzard (55).

Of the cases hitherto recorded ten have been in England, four in America, eight in France, five in Italy, the remainder in Germany and Austria.

It is difficult at present to form an idea as to the frequency of a disease the clinical picture of which is so little known to the medical profession. The condition is undoubtedly a rare one. Erb did not meet with another case for twenty years after his original description.

During the last six months four patients suffering from myasthenia gravis have been treated in the National Hospital, Queen Square.

Etiology.

Males and females are almost equally affected. The age at which the sexes are attacked is different. Of fifty-eight cases the average age was for men 35 and for women 24 years. The youngest patient in whom the disease has been

* Strumpell's cases :—

Wilks (1)	Erb (3)	Eisenlohr (1)
Oppenheim (1)	Shaw (1)	Bernhardt (1)
Jolly (2)	Goldflam (4)	Hoppe (1)
Reinak (1)	Pineles (3)	Strümpell (1)

† Wilks (1) Shaw (1) Dreschfeld (1)
Suckling (2) Clifford Allbutt (1) Guthrie (1)
Harry Campbell (1) Buzzard (2)

observed—excluding a doubtful case in a child aged 2½ described by Mailhouse, (39)—was 12, the oldest patient, 55.

With regard to occupation, no conclusive deductions are to be drawn, although in the majority of instances in which mention of this point has been made the patients have been manual workers.

Rarely has there been a family tendency to nervous disease. Exceptions to this are found in cases recorded by Goldflam (9), Sinkler (50), Buzzard (55), Suckling (15), and Kojewnikov (30). No case is on record in which more than one member of a family has been affected. As frequently as not the malady attacks individuals who have previously enjoyed good health. A considerable percentage of the female patients have been anæmic. Laquer's patient suffered from attacks of gout. In a few instances there have been signs of a defective nervous system. In Berkeley's (34) case there was an obvious mental defect. In a case described by Karplus (37) the patient had recurring ptosis from the time she was 5 years of age. In Saenger's (43) case the patient had infantile paralysis when a child. Eisenlohr's patient as a child suffered from megrim occasionally accompanied by ptosis. With these exceptions there is a striking absence of a nervous or hysterical temperament.

Syphilis and alcohol appear to play no part as causative factors.

Not infrequently the symptoms have followed upon some previous affection, such as influenza (Remak, 12), scarlatina (Campbell, 53), typhoid fever (Sinkler, 50), sore throat (Saenger, 43; Eulenberg, 38), otitis media (Jolly, 20), an attack of diarrhœa (Shaw, 6), and acute intestinal obstruction (Feinberg, 57). In one case the onset of menstruation (Kojewnikov, 30), in others a confinement (Punton, 51, Laquer, 40), appear to have acted as exciting causes. Emotional excitement (Angelini, 49), a chill (Kojewnikov, 30; Clifford Allbutt, 53), the extraction of a tooth (Wheaton, 41) and an attack of megrim (Eisenlohr, 4) have been blamed. In two cases the illness was attributed to taking cold baths (Buzzard, 55; Montesano, 45), in others to over-exertion (Suckling, 15, Buzzard, 55).

Mode of Onset.

The disease usually comes on gradually, although in a few cases the onset has been sudden. Occasionally slight headache, pain in the neck and back, giddiness and photophobia have immediately preceded the first symptoms of motor weakness.

Most frequently the characteristic weakness first shows itself in the muscles innervated by the bulb. Thus, in the case of a schoolboy, the first symptom was an inability to keep the eyes open—he was unable to look at the blackboard on account of the dropping of the upper eyelids. Diplopia, weakness of the lips, indistinct speech, difficulty in masticating and in swallowing, and inability to hold the head erect, have each been met with as the earliest manifestations of the disease. A considerable number of cases have been described in which the limbs were first affected. An hotel cook found that his fingers were weak after rolling dough. Another patient first noticed weakness in the fingers after sawing wood. A housemaid, who had a great deal of "stair work," became very weak in the legs, so much so that on several occasions the legs gave way and she fell to the ground. In some cases the initial weakness is more general, affecting both the limbs and bulbar muscles.

Symptomatology.

Bulbar muscles.—Ptosis is a common symptom; it is usually bilateral and often more marked on one side than the other. Sometimes the ptosis is constant; in other cases it is only present towards the latter part of the day, or if the patient attempts to look up for any length of time, when the upper lids gradually fall. On account of weakness of the occipito-frontales muscles, frontal overaction, which is so frequently associated with the ptosis of tabes and serves to antagonise the drooping of the lids, cannot occur. The only way in which the patient can counteract the ptosis is by throwing back his head, but here again weakness of the neck muscles makes it difficult for him to maintain this position.

Some interesting observations in connection with ptosis were made in Dr. Buzzard's male case. It was observed by Mr. Marcus Gunn that on appealing to the patient's emotions and occasionally upon mental concentration, the upper lids were temporarily raised to some extent, in association with a certain amount of dilatation of the pupils. In the same patient on another occasion, just after he had awakened from sleep, the upper lids were retracted so that the sclerotic was visible above the corneal margin. In this, as in several other recorded cases, von Graefe's sign was at times present. These facts would suggest that the fibres of Müller are not affected.

Weakness of the external ocular muscles with consequent diplopia is often present. Sometimes one muscle is more affected than others, sometimes there is a general paresis affecting all the extrinsic muscles, while in some cases complete and persistent ophthalmoplegia externa has been present. A striking feature of the diplopia in myasthenia gravis is the alteration in the relative position of the two images at different times.

In some cases irregular nystagmoid movements, similar to those seen in conditions of general asthenia, are induced upon conjugate lateral deviation of the eyes. The ocular muscles, as is the case with other voluntary muscles, become readily fatigued; patients frequently complain that after reading a few lines the letters and words become blurred and indistinct, and run into each other.

Pupil changes are quite exceptional. The pupils are sometimes unequal. In one case, recorded by Brissaud and Lantzenberg (36), in which, however, the diagnosis appears doubtful, they did not react either to light or accommodation, while in one or two others the reactions were sluggish.

In Dr. Buzzard's case, already alluded to, after prolonged convergence the pupils showed a great tendency to oscillatory movements. Attempts to tire out accommodation in this case, as in others in which the experiment has been tried, were unsuccessful, nor was it found possible to exhaust the sphincter iridis by holding a bright light in front of the eyes.

Difficulty in masticating is one of the most constant symptoms of the disease. The difficulty may be slight and only noticeable after a meal, and more especially towards evening. Sometimes the weakness of the muscles of mastication is so great that the finger may be placed with impunity between the patient's teeth while he closes the jaws with all the force he can command. Often the mouth is kept slightly open because of the weakness of the elevators of the jaw. In cases in which the weakness of the muscles of mastication is great, there is a tendency for the lower jaw to drop, which causes great distress to the patient. In several cases the patient was in the habit of supporting the lower jaw with the hand while masticating.

In Buzzard's first case a curious symptom, connected with the jaw muscles, was complained of. The patient stated that not infrequently he was wakened from sleep by a champing movement of the jaws, which sometimes resulted in his biting his tongue. This symptom was probably due to a clonic contraction of the elevators of the jaw, and is comparable with the clonic movements which have been occasionally noticed in the extremities. Patients sometimes complain of an increased flow of saliva, probably comparable to the well-known dribbling of bulbar paralysis.

The facial appearance is striking and characteristic. The immobile, expressionless face and the drooping upper lids remind one of the Landouzy-Dejerine form of myopathy. Often there is complete inability to wrinkle the forehead, raise the eyebrows, or to frown. Erb (2), in describing his early cases, draws attention to this upper facial weakness.

The sphincters of the orbit are often so weak that the patient is unable to keep his eyes closed against the slightest resistance. In many cases there is great weakness in the muscles about the mouth. A very poor attempt is made to raise the upper lip and show the teeth; the patient cannot pout the lips, "empty a spoon with the upper lip," whistle, or blow out a candle. In extreme cases fluids dribble from the mouth while drinking. In one case the patient was in the habit of supporting the lower lip with her fingers to prevent this occurring.

Difficulty in swallowing is another symptom which is rarely absent. In several instances death has followed attacks of choking brought on while swallowing. Fluids are, as a rule, more easily taken than solids, although, on account of weakness of the palate, they frequently regurgitate through the nose. One patient, when swallowing, always supported the hyoid bone with her hand. The pharyngeal reflex is often absent, a fact which is probably of importance in explaining this symptom.

Weakness of the palate is of frequent occurrence, the voice becomes nasal, and, if the weakness is marked, fluids regurgitate through the nose when the patient drinks. The patient is unable to blow out his cheeks, the air escaping through the nose. The movement of the palate is almost always impaired and becomes much more feeble after repeated vocalisation of the letter ā.

The palatal reflex is usually diminished, and may be absent.

Paralysis of the laryngeal muscles has been but rarely noticed. In one case there was paralysis of one vocal cord (Punton, 51); in another movement of one cord was defective (Bernhardt, 7). In other cases the tone of the voice has been lowered, suggesting weakness of the adductors.

In Hoppe's case there was weakness of both abductors and adductors. In one case (Dreschfeld, 14) the abductors, in another the adductors were weak (Kojewnikov, 30). In Dr. Buzzard's first case it was remarked by Sir Felix Semon that after repeated deep respirations the cords did not separate so much as at first, clearly showing myasthenic weakness of the abductors. In two cases, those of Wernicke (16) and Toby Cohn (31), anæsthesia of both pharynx and larynx was present.

A feeling of fatigue and of "aching" and "stiffness" in the tongue is often complained of, especially after speaking or eating. The movements of the tongue may be impaired. The patient can usually protrude the tongue, but cannot long maintain it in this position, and he may not be able to thrust out the cheek forcibly with it.

Very characteristic alterations in speech occur. It may

be that the patient speaks naturally when he begins, but soon speech becomes nasal; words become more and more indistinct; the voice becomes weaker and weaker, and finally he has to stop for want of breath. The altered speech is due, in part, to weakness of the articulatory apparatus—lips, jaws, tongue, and soft palate; in part to defective action of the respiratory muscles, which make it impossible for the patient to take in sufficient air for phonation. These peculiarities are well demonstrated when the patient reads aloud.

Trunk muscles.—The myasthenia, as already observed, involves the muscles of the trunk and limbs, as well as those just considered.

Weakness in the neck muscles and consequent inability to support the head is common. In some cases the head tends to fall forwards, in others backwards, and it often requires support.

The muscles of the back may suffer in a similar manner, so that the patient cannot sit up for any length of time without feeling tired. On account of weakness of the abdominal muscles he may be quite unable to raise himself from the recumbent to the sitting posture without using his hands. So marked is the weakness of the trunk and limb muscles in some cases that there is the greatest difficulty in turning in bed.

The muscles of respiration may likewise be involved. In one case the difference between the circumference of the chest at full inspiration and complete expiration amounted to a quarter of an inch only. The dyspnœa, which results on even slight exertion, finds a ready explanation in this fact. Besides the dyspnœa which follows exertion, unaccountable attacks of breathlessness occur, during which the patient is in danger of his life. Strümpell (24) gives a graphic account of the dyspnœic attacks which occurred in his case:—"The patient falls to the ground if walking, becomes cyanosed and breathless. Respiration is noisy and restless; sputum accumulates in the mouth; he can neither swallow it nor spit it out. The tongue appears to sink back into the mouth. If in bed he sits up with head bent forwards, the saliva flowing from his mouth. The

arms when raised fall flaccid to the side." These attacks may persist for several hours. Strümpell believes that they are due to sinking back of the tongue, and in his case he was in the habit of pulling the tongue forward with marked benefit. Attacks of palpitation are not uncommonly complained of, sometimes in association with dyspnœa, at other times quite independently. The palpitation may be entirely subjective and unassociated with any increase in the pulse rate.

Extremities.—It has been pointed out that in the extremities the muscles situated near the trunk usually suffer most. Not infrequently the first weakness in the arms is noticed when the patient undresses at night to go to bed. One of the earliest symptoms in the case of a female patient was inability to raise the arms in order to brush her hair. But the weakness is by no means confined to the shoulder and upper arm muscles. In two cases, already referred to, weakness in the fingers was the first symptom to appear. The handwriting may show characteristic changes dependent upon the myasthenic condition. At first the letters are well formed and the patient writes fairly rapidly, but gradually the writing becomes slower and more laboured and the letters badly formed, until finally he has to give up the attempt. Weakness in the arms may be so great that the patient cannot feed himself. The ilio-psoas and quadriceps would seem to be the muscles which are as a rule most involved in the legs. As a rule the patient is unable to walk a long distance, sometimes he cannot walk fifty yards, indeed, he may not be able to walk at all.

In slight cases the patient appears to walk quite naturally. When the legs feel tired he rests for a minute or two, and then walks on almost as well as before. In cases in which the lower extremities are very weak the gait is waddling in character.

Sudden giving way of the legs is a not infrequent symptom, and was first drawn attention to by Strümpell.

Factors influencing the myasthenic condition.—Emotional excitement increases the intensity of the symptoms in a very striking way. In one of Goldflam's cases a relapse

occurred after a fright. The presence of a strange doctor may be sufficient to intensify the symptoms for the time being. In one case reading an exciting description of a battle produced a similar result.

Buzzard's patient always felt worse in cold weather. In a case under the care of Dr. Ormerod five years ago, which presented many of the features of myasthenia gravis affecting the limbs, the patient, a blacksmith, writes to say that he is now quite well, although in the cold weather he still notices some weakness in his fingers. The myasthenia in Campbell's second case was always increased by cold weather.

Female patients are often worse at the menstrual periods. Such was very decidedly the case in one of our own patients. As we have seen, several of the recorded cases have come on after a confinement.

The speedy production of muscular exhaustion constitutes the most striking feature of the disease. Persistence in a movement causes it to become gradually weaker, and ultimately impossible, until after a short rest, when it can again be repeated.

As Strümpell pointed out, persistent paresis picks out especially those muscles whose function necessitates persistent activity, such as the cervical muscles and the extrinsic muscles of the eyes.

Laquer (40) found that fatigue induced in one group of muscles causes fatigue in others, and Mosso has shown that this is also true of physiological fatigue. Goldflam, on the contrary, in a case which he examined, was unable to demonstrate this point. Observations on Dr. Buzzard's cases support Laquer's conclusion.

The great variations which occur in the intensity of the symptoms from time to time are very characteristic of the disease, and were first called attention to by Goldflam (13). Even in hospital, when a most careful record is kept of a patient's every act, quite unaccountable relapses occur.

Electrical reaction.—Jolly (20) in 1895 drew attention to the peculiar manner in which the muscles react to electrical currents. He found on applying a tetanising current to the

muscles of a patient suffering from this disease a brisk contraction was produced, but that if the electrodes were kept in contact with the muscle the contraction became gradually feebler until finally the muscle ceased to respond. On removing the electrodes and reapplying them again after a minute or two a good contraction was obtained, which disappeared just as on the first occasion. Jolly compared the exhaustion produced by electrical stimulation to that which results after voluntary exertion, and he gave the name *myasthenic reaction* to the phenomenon which he had observed.

The myasthenic reaction is not always present; it occurs in some cases as a passing symptom, in other cases it has not been obtained.

At one time a muscle can be exhausted in twenty-five to thirty seconds by the application of a moderately strong current, at another time it is impossible to exhaust it; a fact not surprising in view of the known variability of the myasthenia from time to time. The comparison between the myasthenic reaction and the myotonic reaction found in Thomson's disease is of interest.

Further, the myasthenic reaction is met with in different muscles at different times.

Murri (25) made the interesting observation that after a muscle has ceased to respond to the faradic current voluntary power still persists, and is only slightly diminished in degree.

The readiness with which the myasthenic reaction can be obtained, as Jolly has remarked, varies with the degree of fatigue in the muscles.

Attempts to exhaust the muscles with galvanism result only in a slight diminution in the contraction.

In cases described by Erb (2), Oppenheim (5), Bernhardt (7), Senator (10), Kojewnikov (30), Montesano (45), Wernicke (16), Pineles (23), and Kalischer (32) diminished excitability was present in certain muscles, notably in those of the tongue, neck, and shoulder. In Kojewnikov's case reaction of degeneration was present in the tongue.

Atrophy.—Although muscular atrophy is altogether ex-

ceptional in this disease, in a few cases it has been met with. Some of the recorded instances have probably been cases of polio-encephalitis (superior nuclear palsy), but others—and such cases are of extreme interest—have presented the classical features of myasthenia gravis.

In one of Erb's cases the masseters were atrophied. Atrophy of the tongue has been described by Erb (2), Dreschfeld (14), and Kojewnikov (30). In Dreschfeld's case there was some degree of atrophy in the sternomastoids, trapezii, and deltoids. In Kojewnikov's case the face muscles were manifestly atrophied, while both masseters, especially the left, were very atrophic.

In Kostetzki's (47) case the pectorals, deltoids, thenar and hypothenar eminences, glutei and spinal muscles, were atrophied. In this case, however, the diagnosis was not quite clear, the writer regarding it as a transition form between chronic bulbar paralysis and asthenic bulbar paralysis. One of Laquer's (40) cases is of the greatest importance in this relation, for in it atrophy of the deltoid, biceps, triceps, pectorals, interossei, quadriceps, and calf muscles, developed while the patient was under observation.

Fibrillary contraction was present in the tongue in cases recorded by Erb (2) and Senator (10), but in no other region has it been noticed.

In some cases occasional chronic spasmodic jerks occur in the extremities; this was so in Buzzard's female case (55).

The muscular sense and co-ordination are never impaired.

With the exception of a feeling of fatigue in the muscles after they have been exercised, and of stiffness due probably to immobility, sensory symptoms are seldom present. Sometimes patients complain, even when lying in bed, of an aching in the limbs, and this, like the stiffness, is probably connected with the immobility of the affected parts. The muscles are sometimes tender on pressure; no other objective sensory disturbance occurs.

The skin reflexes are in no way peculiar. A jaw-jerk is sometimes present. The triceps- and biceps- jerks are, as a rule, brisk, although in some cases it is difficult to elicit them.

The knee-jerks are usually rather more active than normal. In a case described by Collins (26) it was found possible to abolish the knee-jerk by seven or eight strokes on the patella tendon. In one of Goldflam's cases a similar condition was present, while in Strümpell's case the activity of the knee-jerk appeared to diminish somewhat. In other cases the knee-jerk did not diminish after repeated tapping (Laquer, 40; Angelini, 49; Buzzard, 55). The knee-jerk does not diminish if the quadriceps is fatigued. In one of Buzzard's cases exhaustion of the vastus internus by faradisation produced no effect on the knee-jerk. Ankle clonus is not met with. The plantar reflex, where it has been tried, gives a flexor response.

The sphincters are never affected in this disease. No trophic changes occur in the bones or skin.

Morbid Anatomy.

In the great majority of cases in which an autopsy has been made no lesion has been found.

Of seventeen cases which have come to the *post-mortem* table, in only six was anything abnormal found which could *possibly* account for the symptoms, notwithstanding that in many of the cases the most modern methods were used, and the microscopical examinations made by highly skilled observers.

Two cases described by Mayer (18) and Kalischer (32) respectively, deserve special attention in this relation. Mayer's case appears to have been an undoubted example of the disease. The patient had speech trouble, difficulty in swallowing, weakness of the jaw muscles, double ptosis, and paresis of the extremities; there was no atrophy, and the reflexes were normal; towards evening and after exertion all the symptoms were most pronounced; temporary improvements and relapses occurred, death ultimately occurring by choking. Microscopical examination showed that the cells of the hypoglossal nucleus, with the exception of a small number which contained vacuoles, were completely normal, as were those of the anterior horns. A morbid

condition of the intra-medullary portion of the anterior roots, as well as the hypoglossal root, was present, particularly well seen in Marchi preparations. Undoubtedly the condition of the nerve sheaths was pathological, but to what extent the axis-cylinders were affected could not be determined.

In the case which Kalischer describes, the diagnosis is not absolutely certain. Jolly (20) believes it to have been a case of myasthenia gravis, but Strümpell (24) is not convinced. A description of the case will be found in the appendix. Kalischer found degenerative changes in the cells of the motor gray matter from the oculo-motor nucleus, through the whole length of the cord to the sacral region, the fine fibres of the gray matter being rarified. Small hæmorrhages were seen round the dilated blood-vessels in this region. The vessels had in places undergone changes, the adventitia was thickened, and here and there aneurismal dilatation of the lumen was present.

Widal and Marinesco (33) have recorded a case in which, besides dilatation of the vessels, a partial disappearance of the chromatophilic elements in the nerve-cells of the third, sixth, seventh, and twelfth nuclei existed. Degenerated fibres were demonstrated by the Marchi method in the third, seventh, and twelfth nerve-roots. This case again is not quite typical, for death, which occurred suddenly fourteen days after the first symptoms were noticed, was preceded for eight days by slight fever.

In a case reported by Murri (25), numerous hæmorrhages were present and chromatolysis in some of the cells of the hypoglossal nucleus. Cohn disregards the cell changes found in this case, since the *post mortem* was not made until six days after death.

In two cases (Eisenlohr, 4; Wernicke, 16), recent hæmorrhages were found in the medullary nuclei. These patients died, the one of paralysis of the diaphragm, the other suddenly of asphyxia, and it is possible that the hæmorrhages were produced in the act of dying. In another case, described briefly by Charcot and Marinesco (22), in which recent hæmorrhages were met with beside

the aqueduct of Sylvius and about the ventral nucleus of the vagus, the patient died with "bulbar symptoms."

Such cases are, however, exceptional, and, as already observed, in the majority of cases no visible lesion has been met with after death. In the few cases in which changes have been present, these changes, as Kalischer (32) and Laquer (40) have pointed out, were not present in all those centres whose functions showed signs of disturbance during life. Changes, no doubt, are present, although it may be that they cannot be demonstrated by our present methods; but it is open to question whether those hitherto described are actually the cause of the symptoms which the patients manifest during life. It is of great importance that in future careful examination be made not only of the multipolar cells, but also of the muscles themselves, of the nerve-endings in the muscles, of the motor nerves, nerve-roots and cortical cells.

In the few cases in which the muscles have been examined no changes have been found.

Seat of Lesion.

It can be readily understood that in the presence of such a meagre morbid anatomy, various views are held as to the seat of the lesion.

As Strümpell states (24), there is not a single case which is associated with symptoms pointing to parts other than the motor nervous system, and so much seems to be admitted by all observers. Collins (26), although he admits that the phenomena of the disease are largely manifested through the motor system, is inclined to regard the condition as due to an affection of the sympathetic. He bases his opinion upon the attacks of collapse and cyanosis from which his patient suffered.

Jolly (58) concludes from the myasthenic reaction that an abnormal condition exists in the muscles themselves. There are, he contends (58), no certain facts proving that the disease is one of the central nervous system.

Mendel (58) thinks that the occurrence of sudden death

in some cases is opposed to the view that the disease is always a purely muscular affection. Strümpell (24) argues from the myasthenic reaction that the affection is not limited to the upper motor neuron.

It is not possible, with the facts we at present possess, to make any definite statement as to the part or parts of the neuromotor apparatus involved by the morbid process.

Pathology.

We are equally ignorant as to the true pathology of the disease. It has been suggested, and this view is very generally accepted, that the disease is due to some toxic agent, the result of a disturbed metabolism. Laquer strongly supports this metabolic theory, and he points out with regard to physiological fatigue that the preservation of normal muscle excitability is dependent upon a suitable change between rest and activity, that long-continued activity, resulting in the complete loss of irritability, is the condition in fact which we call fatigue, and that the appearance of fatigue depends upon the existence of products of decomposition out of the muscle substance itself which accumulate in the blood.

Collins (26) thinks that the most plausible theory of the pathogenesis of the disease is that a poison is generated in the system and continuously operates on the vegetative portion of the body. When vitality is sufficiently low to let the poison get the upper hand a relapse occurs.

It may be, however, that the toxine is of exogenous and not of endogenous origin. As Strümpell points out (24), the absence of any family tendency and the onset in some cases after an acute illness are in favour of this view.

In regard to the pathology of the disease it is impossible at present to do more than surmise. The view we ourselves put forward is that the disease is due to a poison probably of microbic origin acting upon the lower motor neurons and interfering with their functional activity without necessarily producing discoverable change in structure. We suggest that the poison acts upon the motor fibre (= axon) or end

plates; as to whether it also acts upon the cell-body (in bulbar nuclei or anterior horns), we can form no opinion.

The evidence in favour of a toxine being the pathogenic agent is strong. The symmetry of the affection is alone highly suggestive of this view; also the fact that it occurs in connection with disease in which nerve poisons are known to be produced. Thus cases occur after such diseases as scarlatina, influenza, sore-throats, typhoid fever, which are well known to be often followed by toxic neuritis. Other cases have occurred after otitis media, others have begun with diarrhœa, both of which diseases may be associated with blood-poisoning. We have ourselves seen Laundry's paralysis originate in an acute gastro-intestinal attack with profuse diarrhœa, undoubtedly due to ptomaine poisoning, the poison in this instance apparently paralysing, like urari, the motor end organs. Megrim, again, is a disease which is almost certainly toxically induced, and it is noteworthy that one of the cases of myasthenia gravis occurred in a megrimous patient immediately after an attack of megrim.

It is now fairly well established that tabes dorsalis is a toxic disease, the poison acting chiefly upon the sensory periphery, but also to some extent upon the lower motor neurons, causing the Argyll-Robertson phenomenon, paresis of the extrinsic ocular muscles, and the levators palpebrarum. Now, in the case of the latter muscles, the paresis is often transient; moreover, we have observed the fatigue phenomenon in these cases. Seeing then that transient paralysis and the fatigue phenomenon may be brought about by a toxin, it does not seem improbable that myasthenia gravis may be similarly induced. Assuming the disease to be produced by a toxin, we have to inquire whether the poison is endogenous or exogenous. We know that substances normally present in the body may cause fatigue, and conceivably myasthenia may be due to an excess of such poisons —poisons, namely, produced by the metabolism of the organism. The occurrence of the disease after such maladies as influenza, scarlatina, typhoid, and sore-throat suggests a microbic origin.

The poison may conceivably act upon the motor nervous

system, or upon the muscles themselves. In the former case it might involve the upper or the lower neuron or both.

Several arguments may be adduced against the upper neuron being the essential seat of the lesion. The myasthenic reaction and the exhaustibility of the knee-jerks, as met with in Collins' case, the occasional atrophy and diminished faradic excitability, cannot be explained on the assumption of an upper neuron-lesion alone. Nor can we in this way explain the tendency to spontaneous attacks of dyspnœa, attacks so severe as to frequently prove fatal. Nor, again, the tendency to choking from pharyngeal paralysis, seeing that the choking is essentially due to defect of the voluntary part of the act of deglutition. Further, the attacks of palpitation are in no way suggestive of a lesion in the upper motor level. One cannot, indeed, fail to detect a likeness between the attacks of dyspnœa, choking, and palpitation met with in myasthenia gravis, and similar attacks occurring in affections of the lower motor level, to wit, bulbar paralysis and peripheral neuritis—the diphtheritic form, for instance.

But perhaps the most conclusive evidence against the view that the essential lesion is situated in the upper motor neuron is afforded by the myasthenic reaction; the muscles in myasthenia gravis become unduly exhausted by faradic stimulation, the same fatigue being experienced as occurs after voluntary action in this disease. It is evident that this phenomenon must be due to a peripheral cause.

We have next to consider whether the disease involves the lower motor neurons or the muscles. On the assumption that it is of toxic origin, it seems safe to exclude the muscles from an essential share in the pathological process. We have no facts in pathology suggesting that a poison can exist in the blood in sufficient quantity to seriously impair the functional activity of the entire muscle system, and this without producing any other symptoms, much less that such a poison can pick out symmetrical muscles, *e.g.*, the levators palpebrarum, to the exclusion of all others. What we know of the action of drugs and toxins strongly suggests that if

myasthenia gravis is due to a *poison*, acting selectively, it produces its effects by acting upon nerve rather than upon muscle.

The myasthenic reaction, while it does not enable us with certainty to fix the lesion upon nerve rather than upon muscle, yet lends support to the view that the former is involved. On this assumption the motor-fibre, end-plate, or muscle-fibre may be implicated. The characteristic reaction is obtained by faradism, not galvanism. Now faradism causes contraction essentially through the nerves; its power of causing contraction by direct stimulation of the muscles is small. The inability of galvanism to cause the exhaustion does not help us, since it contracts the muscles both through the nervous system and by direct muscle stimulation; this inability is doubtless due to the fact that it cannot induce tetanus. The crucial test would be to find if, after inducing complete myasthenia by faradism, the myasthenic muscles respond to galvanism. Such response would afford fairly conclusive evidence that the exhaustion was one of the motor nerve-fibres or end organs.[1]

We have then arrived thus far: the motor end-fibres or end-plates are especially involved in myasthenia gravis. Is the body of the neuron also involved? We can conceive of the toxine acting upon the whole of the lower motor neuron, cell-body, axon, and end-plate. It is indeed possible that it may act primarily upon the cell-body, the axon being secondarily affected through withdrawal of the normal trophic influence emanating from the cell-body. The muscle-atrophy and diminished faradic excitability which sometimes occur prove that the lower motor neuron is, at least occasionally, involved.

[1] We have, at present, no marked case of myasthenia gravis under observation upon which to make this observation. On the suggestion of one of us (H. C.), Dr. Farquhar Buzzard kindly undertook the following experiment:—In a well-marked case of myasthenia gravis a moderate galvanic current was applied to the biceps muscle and a contraction obtained. The muscle was then faradised until it gave no response to a strong stimulus. Then it was tired out by making the patient flex the elbow against resistance, exerted until all power of flexion was lost. On applying the same strength of galvanic current as used at first an excellent contraction was obtained. Finally, on again applying the faradic current, the muscle was found to be still irresponsive.

The fact that discoverable lesions are generally absent *post mortem* is just what we should expect from the symptoms of the disease. Were a permanent organic lesion present we should not expect such marked variations in the degree of paresis to occur as characterise the disease—complete ability to move the muscles one moment, absolute paralysis of them a few moments later, or an entire disappearance of the symptoms for weeks, months, or years together.

What we know of the action of drugs entirely supports the view that function may be profoundly modified by the action of chemical substances, without any discoverable organic change being wrought. Nothing is more certain than that antagonistic poisons may set up a countless variety of transient perturbations in the nervous system. Witness, *e.g.*, the nervous phenomena observed in dyspepsia, and among these it may be observed that lassitude and muscular fatigue are not infrequent.

But while numerous nervous symptoms may result from blood-poisoning independently of discernible organic lesion, it is a fact that in all cases hitherto known to us of paralysis thus resulting, a well-marked lesion is discovered *post mortem*; we allude to such diseases as peripheral neuritis and poliomyelitis. And herein lies the pathological interest of myasthenia gravis. In it we have, we would suggest, an instance of a toxic paralysis, lasting intermittently for a long period of time, and often terminating in death, and in which, nevertheless, no discoverable lesion is necessarily induced. The wonder is not that such cases are rare, but that they are not more frequent. Purely functional nervous symptoms of toxic origin, such as numbness, tingling, twitching, drowsiness, coma, are common enough; why should not purely functional toxic paresis be equally common? As a matter of fact, we believe that such pareses are not altogether uncommon in a very mild form, more especially in connection with dyspeptic toxæmia.

What we suggest, then, is this—that in myasthenia gravis, a toxin, probably of microbic origin, circulates in

the blood, and acts selectively upon the lower motor neuron, so as to modify its functional activity. This change in functional activity is such that the lower neuron soon becomes exhausted by the transmission down it of stimuli, whether originating in an act of will or started by the faradic current. As to which part of the neuron the poison acts primarily upon one can only vaguely surmise; but we lean to the view that it is upon the axon. This brings the disease into line with such a disorder as diphtheritic neuritis. Imagine an attenuated toxin, such as causes this latter disorder, to remain for some time in the body, and the effect might be much the same as is observed in myasthenia gravis. In the earlier stages of the disease no organic changes would be produced, but after prolonged action one might expect such changes to occur, and be accompanied by atrophy of the muscles and diminished faradic excitability.

Diagnosis.

The diagnosis in well-marked cases of myasthenia is easy. The paresis and speedy fatigue of voluntary muscles on exertion, the myasthenic reaction, the absence of muscular atrophy and of fibrillary tremors, of objective sensory disturbance, trophic changes and sphincter affection, together with the remarkable variations in the intensity of the symptoms—form a distinct clinical picture.

A diagnosis can often be made at first glance from the facial expression, the ptosis, and nasal speech.

The diseases most liable to be confounded with myasthenia gravis are hysteria, bulbar palsy, polioencephalitis, the muscular distrophies, amyotrophic lateral sclerosis and general asthenia.

No doubt in hysteria and neurasthenia ready fatigue after exertion is met with, while the variations in the symptoms, the presence of ptosis, difficulty in swallowing, and attacks of breathlessness, all occur. In such cases absence of a nervous heredity and hysterical manifestations, the absence of sensory symptoms and the presence of the

myasthenic reaction, should enable a diagnosis to be arrived at.

Cases undoubtedly occur in which the diagnosis is very difficult.

A case recently seen by one of us illustrates the difficulty which may arise in diagnosing early cases. The patient was a young married woman, who for three years (since her last confinement) had suffered from general muscular weakness. When first seen, after ascending a long flight of stairs, she was much exhausted and very breathless, speech was somewhat nasal in character, and she had slight double ptosis. She complained of general exhaustion after any slight exertion, had had definite diplopia on several occasions, and said she had been very anæmic ever since her confinement. No weakness in the jaws or trouble with deglutition existed, and although the symptoms were very suggestive the facts did not justify a certain diagnosis, especially in the presence of a marked anæmia.

In the myopathies fatigue after exertion is often complained of. We have already seen that the facial appearance is very similar to that seen in the Landouzy-Dejerine form of myopathy. The waddling gait and the tendency for the paresis to affect the proximal muscles of the extremities are other points of similarity; but, as Oppenheim (58) remarks, the resemblance is superficial only, for it is only in myopathic patients, who show the fatigue phenomenon, and those in whom the muscles are only slightly wasted, that any confusion is likely to arise (Jolly, 58). Toby Cohn (58) argues from Laquer's case, in which muscular atrophy developed, that the relation to the myopathies is closer than would appear at first sight.

Wernicke's case (16) was diagnosed at first as one of amyotrophic lateral sclerosis with bulbar symptoms, the absence of muscular atrophy being specially remarked upon.

From bulbar palsy the disease distinguishes itself by the presence of ptosis, upper facial weakness, paresis of the jaw and neck muscles and of the extremities, and by the myasthenic reaction. The variation in intensity of the symptoms is a diagnostic point of great importance.

Lastly, the differentiation from polioencephalitis has to be considered. Here the diagnosis may be extremely difficult. The mode of onset, absence of muscular wasting, and above all the variability of the symptoms, are points to which especial attention must be directed.

Prognosis.

Of sixty recorded cases twenty-three ended fatally.

The average duration of life of the fatal cases was about a year and a half after the development of the first symptoms.

These figures probably give an exaggerated impression as to the fatality of the disease.

In one case, that of Widal and Marinesco (33), death occurred fourteen days after the first symptoms were manifested. In Dreschfeld's case (14) the patient lived fifteen years.

That cases improve in a remarkable way and remain free from symptoms for months, or even years, is certain. That complete recovery sometimes takes place is probable. Goldflam (9) described his cases as belonging to "a curable form of bulbar paralysis." In one of Erb's cases (2) the patient was in good health four years after his symptoms had disappeared. In some cases the disease lasts a number of years.

Involvement of the respiratory muscles, with consequent attacks of dyspnœa, is a symptom of the gravest significance, and the patient's friends should be warned that death may occur suddenly during one of these attacks.

Any pulmonary disorder, whether chronic or acute, is to be considered as of very serious import.

Treatment.

No specific treatment is known for the disease. The patient must be enjoined to take as much rest as possible, and in severe cases should be confined to bed.

Excitement of every sort is to be avoided, inasmuch as the symptoms are much increased by it.

Since cold appears, in some cases at least, to aggravate the disease, attention should be paid to the patient's clothing. Cold baths are to be avoided. The patient's whole life is to be regulated so as to avoid muscular fatigue.

The diet should be nutritious, and if there is any difficulty either in deglutition or mastication, the food is to be carefully chopped, to obviate the necessity for chewing, and to avoid, as far as possible, the risk of choking.

In the event of the necessity arising for using the stomach tube, the greatest care must be taken, for, as in other forms of bulbar palsy, the procedure is not unattended with risk; indeed, in a case reported by Oppenheim, a fatal result followed the passage of the tube.

As to drugs, little can be said. Erb and Goldflam's cases were treated with iodide of potassium and mercury, but there is no evidence to show that this treatment actually has a beneficial effect.

Strychnine was employed by Strümpell (24) in large doses without result. In Buzzard's cases hypodermic injections of strychnine up to one-sixth of a grain in the twenty-four hours were given without benefit.

Faradism, galvanism, and massage were all given an extended trial in Buzzard's male case. Faradism appeared to do harm, the patient feeling weaker as the result of the treatment, while galvanism and massage did no good. Galvanism to the spine has been recommended by Erb (2) and Goldflam (13), but appeared to have no positive value in the case already referred to.

Suprarenal extract was also ineffectual. Under thyroid tabloids, together with a daily injection of five minims of solution of strychnine, the patient improved so much that after six weeks he felt almost well. The improvement began on the day the thyroid was commenced, but it is quite possible that suggestion may have accounted for the success which attended this line of treatment; the case relapsed while still taking the tabloids.

In another case thyroid extract was given without benefit.

Iron and arsenic appear to be of use as general tonics, although they have no specific action upon the disease.

NOTES OF SIXTY REPORTED CASES OF MYASTHENIA GRAVIS.

Case 1, Wilks (1).—A stout girl, looking well, came to the hospital on account of general weakness; she could scarcely walk or move about, she spoke slowly and had slight strabismus. She remained in this state about a month, being neither better nor worse; every movement of her limbs and her speech were performed so slowly and deliberately that the case seemed rather one of lethargy from want of will than an actual paralysis.

At the end of this period the symptoms became aggravated, and in about three days they had assumed all the well-marked characters of bulbar paralysis. She spoke most indistinctly, swallowed with great difficulty, and was quite unable to cough. The limbs were, however, not paralysed, she was able to get out of bed. It was shortly afterwards seen that her respiration was becoming affected, the difficulty of which rapidly increased and in a few hours she died.

The medulla oblongata was very carefully examined and no disease was found. It appeared quite healthy to the naked eye, and the microscope discovered nothing abnormal.

Case 2, Erb (2).—Man, aged 55. Illness developed slowly with pains in the nape of the neck; after four months he could not hold his head up; the muscles of mastication were weak, and he had double ptosis. Thereupon ensued weakness in the tongue and difficulty in swallowing; the mouth was kept open. There was atrophy of the neck muscles and trapezii, and slight diminution in the response to faradism in the trapezii, masseters and splenii. There was a high degree of auditory hyperæsthesia on the left side. Decided improvement occurred after a six months' course of galvanism. He could hold his head up, swallow well, and masticate much better. After a few months he became well, though he still had occasional weakness in the arms.

Case 3, Erb (2).—A peasant woman, aged 30, was seen on October 30, 1870. For nine weeks she had had slight twitchings in the face, diplopia and ptosis; later, difficulty in mastication, stiffness in jaws, much headache and giddiness developed; recently, she has suffered from palpitation and weakness in the limbs. She has had blinking of the eyes and twitchings about the mouth for a month.

State.—The eyes are half closed, the movements of the eyeballs are very defective, there is no diplopia, she has difficulty in

opening and closing the mouth, the mouth is constantly open, and there is some stiffness and weakness of the facial muscles. A feeling of weakness exists without actual loss of power in the lower extremities. She has some left auditory hyperæsthesia.

November 4.—The symptoms are worse. She complains of difficulty in swallowing, and of a profuse salivary flow.

November 10.—There is improvement in the eye muscles and muscles of mastication. She says that for many weeks the head has felt heavy and she has had difficulty in holding it up, while there has been a feeling of weakness in the posterior cervical muscles.

December 22.—Great improvement.

January 17, 1891.—She is slightly worse. The tongue appears atrophied. During the next month fluctuations in the severity of the symptoms occurred.

July, 1891.—Is much worse again. She now has ptosis, diplopia, difficulty in mastication, and atrophy of the masseters. The movements of the soft palate are sluggish; speech is nasal; utterance difficult; the voice is weak, especially after lengthy speech. There are great weakness and fatigue in the legs; she has frequent palpitation. Pulse 100.

Improvement again occurred, but later she became worse and died suddenly on the night of April 24, the illness having lasted eight months. There was no *post mortem*.

Case 4, Erb (2).—A merchant, aged 47, was seen on July 11, 1871. During the last year he had suffered from pain in the occiput, and stiffness and weakness in nape of neck. Since April last he has had sharp pains in head and nape of neck, vertigo and occasional dimness of vision. Towards the end of May weakness in the arms and legs compelled him to remain in bed; he could with difficulty hold his head up. In June he developed double ptosis and was very sleepless; during the last few weeks has been better.

Present condition.—A powerful man. He has slight paralysis of the upper face, he cannot wrinkle the forehead well and there is slight twitching of frontalis. The head is bent forward. The right side of the palate is weak; swallowing is unaffected, but there is occasional fatigue of masticatory muscles. Walking soon causes fatigue, while vertigo and dimness of vision occur after walking much.

No improvement followed fourteen applications of galvanism.

Case 5, Erb (2).—A male, aged 48. His previous health was good. Six months ago the lips felt stiff, and he had

headache and diplopia. Three weeks later he had pain in the neck and the head fell forward, later there was difficulty in chewing and swallowing. Pain and weakness in arms and legs, giddiness and ringing in the ears developed. The voice became hoarse and the movements of the tongue difficult, while ptosis developed.

Present condition.—He has difficulty in speaking, chewing and swallowing. The pupils react normally, the extrinsic eye muscles are unaffected. There is weakness in the right arm, and fatigue is easily produced. He has severe pains in both arms and legs at times. Fibrillary twitchings are seen in the tongue, which is slightly atrophied.

The patient went out of the Klinik much improved after fifty-two applications of the galvanic current.

Case 6, Eisenlohr (4).—A girl, aged 18. *As a child she had suffered from megrim.* This was *occasionally accompanied by ptosis. Two years ago she developed sudden diplopia,* which disappeared after a three months' course of iodide, but returned in the summer of 1885; sometimes chiefly on one side, sometimes on the other. In July, 1886, after an attack of megrim, she had weakness of both hands. In August there developed slight weakness of the legs, breathlessness on quick movement, and difficulty in swallowing, chiefly at midday and in the evening, also weakness of cervical and masticatory muscles. All these symptoms varied in severity even in the space of a single day.

August 16.—The patient was examined. She has ptosis, chiefly left-sided, with little movement of the eyes; can only close the eyes feebly; there is double facial weakness and little movement of the soft palate; she can only swallow small quantities of fluids, which readily regurgitate through the nose; she has great difficulty in moving the head; the respiratory movements are defective and the cough is weak; there is paralysis of all four extremities; swallowing is easy in the morning, difficult in the evening, and movements of tongue are fatiguing. Respiration is superficial; pulse frequent.

August 18.—Palpitation; pulse 140; frequent respirations with fruitless efforts to expectorate accumulation of mucus, &c., from the throat.

August 21.—The diaphragm is almost entirely paralysed. Death.

Post mortem.—The cortex cerebri was not examined. Hyperæmia with small recent *ante-mortem* extravasations was found in the medulla, numerous small but not degenerated fibres

(fasern) in the roots of the hypoglossal vagus and accessorius were observed.

Case 7, Oppenheim (5).—A maidservant, aged 29, seen February, 1885. *Nine months ago she noticed weakness in the hands*, which gradually increased and involved the legs also. For the last four weeks she has noticed fatigue during speaking and has often to pause, also weakness of lips and difficulty in swallowing.

Present condition.—There is little movement of the facial muscles during speech; voluntary movement of the lower face is very defective; there is weakness in opening and closing the jaws; mastication rapidly causes fatigue; she cannot move the lower jaw laterally; there is defective movement of the soft palate during phonation; there is tremor of the tongue with defective movement; speech is nasal. She cannot cry out; inspiratory movements are defective; she complains of breathlessness; there is great weakness in arms and in the abdominal muscles; she says that the degree of weakness in the extremities varies greatly from time to time. Sight is normal. There is no muscular atrophy, no electrical change, but the deltoid and biceps require unusually strong currents to excite contraction.

June, 1885.—Manifest dyspnœa. In the following month attacks of difficulty in swallowing and speaking developed.

August, 1885.—She has weakness in the orbicularis palpebrarum, and attacks of dyspnœa; the paralysis is increasing with slight remissions.

January, 1886.—She complains of pains in nape of neck, occasionally in the extremities and face.

May, 1886.—There is increased weakness in extremities, she can scarcely hold her head up.

September, 1886.—She died in a dyspnœic attack with pneumonia.

Case 8, Lauriston E. Shaw (6).—A baker, aged 37. He had enjoyed good health until the present illness. Six months ago he had a severe attack of diarrhœa lasting a fortnight. Ever since then he had had a feeling of weakness, especially in the muscles of mastication, the arms, and to a less extent, in the legs. After this difficulty in articulation and swallowing supervened. The weakness was slight in the morning and increased as the day advanced. He has had two attacks of dyspnœa within the last fortnight; there has been a copious secretion of frothy mucus with difficulty of expectoration.

Admitted, February 12, 1887.—He can barely stand; he says

he often falls down. The soft palate is normal. The mouth is constantly held slightly open. There is loss of power in the lower facial muscles. The naso-labial fold is obliterated, causing a vacant expression. There is some difficulty in protruding tongue; the masseters are weak; he cannot hold a pipe either with the lips or teeth; has difficulty in swallowing and occasional diplopia; the tendon reflexes are brisk; spurious ankle clonus is present on the right side; the cremasteric and plantar reflexes are normal, the abdominal and epigastric absent. The mental condition is good; he has perfect control over the bladder and rectum.

He died shortly after admission from dyspnœa, apparently resulting from paralysis of the muscles of respiration.

Post mortem.—Pons, medulla, and cord were examined by Dr. Newton Pitt, and nothing abnormal discovered.

Case 9, Bernhardt (7).—A joiner, aged 44. In August, 1886, he first complained of fatigue and weakness in the eyes, later he had diplopia.

Present condition.—November, 1886. There is double ptosis, on the right side chiefly; the left external rectus is paralysed. After chewing for a short time he cannot close jaws. Under potassium iodide and galvanism he was dismissed cured in February, 1887, and continued well till 1890.

July, 1890.—The head falls forward on chest, chewing and swallowing are difficult, and speech soon becomes nasal; the lips are fatigued after continued speech, and work easily exhausts him. Movements of the arms are difficult; there is slight right ptosis; the electrical reactions are normal, but there is slight quantitative diminution in the neck muscles.

September, 1890.—He has dyspnœa on walking quickly, or on mounting steps. *The right vocal cord moves less readily than the left.* He improved under potassium iodide and electrical treatment.

1890.—Sudden death occurred. No *post mortem* was allowed.

Case 10, Jolly (8).—A tanner's apprentice, aged 15, was admitted on August 19, 1890. The family history was unimportant. He had suffered from middle ear disease for a few years, and had had no other illness of importance. His present trouble began eight months ago with weakness in the legs; later, weakness in the arms, difficulty in speaking, giddiness, and pain in the neck and sacrum developed. After walking a short distance he requires support to prevent him falling. He has double

ptosis; fatigue soon develops after whistling, speaking, chewing, or swallowing; the eye movements are good. The knee-jerks are somewhat increased. There are no qualitative electrical changes, but the quantitative estimation is peculiar, the muscles at first respond well, but if the same muscle is stimulated repeatedly so that a tetanic contraction is produced, the contraction of the muscle gradually becomes weaker until it is only elicited by very strong currents—in other words, the reaction of fatigue is present.

The patient died suddenly on March 18 while eating, a piece of food sticking in his throat. At the autopsy nothing abnormal was found either in the nervous system or muscles.

Case 11, Jolly (8).—A boy, aged 14, who had been strong and healthy until the summer of 1893. At that time (one and a half years ago), while at school he noticed that he could not see the black-board properly, for he was unable to keep his eyes open, the eyelids drooping if he looked at an object for any length of time. After a rest, and particularly in the morning, this was not the case. Later, tiredness of the legs, also of the arms, of the neck and lip muscles, appeared. While eating he had to stop frequently because he could not go on chewing. If he read aloud, speech became indistinct, reminding one of general paralysis; there was no affection of the tongue or of swallowing. All voluntary muscle was readily exhausted, and also the exhaustion of one group of muscles was seen to produce fatigue in others; if, for example, the legs are tired, then the arms become fatigued, though not to the same degree.

Case 12, Senator (10). (*Doubtful case.*)—A workman, aged 41. Twenty years previously he had an ulcer on the penis and swelling of glands; no other evidence pointing to syphilis. Been feverish for nine weeks and had a slight cough, rigors, heats, sweats, and nasal speech. On the night of November 27 and 28 he had difficulty in swallowing and speaking, tongue was immobile, and there was little power of moving the jaws, a fixed expression, and the eyes seemed large. November 29 he could not move his right arm, there was a tendency to walk to the left and he drags the right leg.

Present condition.—He cannot speak; pulse 64; respiration 28. He can only move the right arm slightly; the right leg is paralytic; the plantar and patellar reflexes are active; rather more on the right side. There is paralysis of all the muscles supplied by the facial nuclei; laughing and whistling are im-

possible. He cannot close his eyes properly. He keeps the mouth half open and cannot powerfully close it. The lateral movements of the jaw are unaffected; the tongue is motionless; he has great difficulty in swallowing; the electrical reactions are normal, but the left facial muscles require a stronger current than the right. Involuntary twitchings of the mouth occur; there is diminished movement of the soft palate; the eyeballs are prominent.

The condition gradually improved with slight fluctuations till February, 1885, when he got worse. Death occurred from exhaustion in March, four months after beginning.

Post mortem.—A microscopical examination of the base of the brain, cord, peripheric nerves and muscles, revealed nothing morbid.

Case 13, Senator (10). (*Doubtful case.*)—A woman, aged 36. She is very anæmic and is suffering from sarcomata of the ribs. She developed in the course of the illness a nervous affection, pains in the head, back, and lower extremities, together with a feeling of fatigue. At this time albumosuria was first detected. She complained of difficulty in swallowing; she said that her chin felt as if it were dead and "did not belong to her." It was found to be quite anæsthetic. The tongue was almost completely paralysed; it was not atrophied, though fibrillary twitchings often seemed to occur about the middle of the tongue. The pulse rate was increased. The electrical reactions in the face and lower limbs were normal; in the tongue excitability was diminished. Death occurred somewhat suddenly.

At the *post mortem* multiple sarcomata of the ribs, double fibrinous pleurisy and chronic parenchymatous kidneys with waxy change; neither in the brain nor medulla was anything found to account for the condition.

The severe anæmia, Senator thinks, may have produced the symptoms by acting upon an imperfectly developed nervous system. Senator remarks that nervous symptoms have been present in several cases of multiple myeloma, *e.g.*, in Stockvis's case there was defective speech and swallowing, together with salivation, paralysis of the facial and trigeminus nerves, and paraplegia.

Case 14, Hoppe (11).—A blacksmith, aged 40, family history good, no syphilis. The illness began by double ptosis, followed by weakness of the muscles of mastication, and difficulty of speech and swallowing. Examination showed paralysis of the

right internal rectus and left superior rectus, the upper and lower part of the facial; great weakness of the masticatory muscles; little movement of the soft palate, paralysis of adductors and abductors of vocal cords; great weakness of the extremities.

The electrical reactions were normal, and there was no muscle atrophy.

The patient died, and no pathological lesion was found *post mortem*.

Case 15, Remak (12).—A girl, aged 12. She had influenza in February, 1890, with suppuration of the left ear. In July it was noticed that the eyes did not close during sleep, and speech was often indistinct. In September she complained of difficulty of swallowing. She had a fixed facial expression, the tongue was weak and the soft palate sluggish. Speech was nasal and indistinct, and after speaking a little while she could not articulate at all because of weakness in the tongue and lips. The difficulty in speech and swallowing improved under galvanic treatment. She had difficulty in getting up expectoration, and often dyspnœa.

October 6.—There is slight tremor of tongue, she cannot raise the tip.

October 16.—She has slight weakness of the arms.

October 21.—Pulse 120. Severe dyspnœa in consequence of weakness of the respiratory muscles; swallowing is impossible.

November 5.—Intense dyspnœa; death. No *post mortem*.

Case 16, Goldflam (13).—A male, aged 25, house-servant, was seen on December 22, 1891. His illness began suddenly seven weeks ago, with headache, giddiness and limitation of the movements of the head. A week later disturbance of speech and swallowing set in, followed by weakness in the arms—a few days later in the legs. Recently he has had severe pains in the shoulder and sacrum. There is no history of syphilis or alcohol.

Present state.—A fairly well-developed man; his speech is nasal. There is very little mobility of the soft palate; the pharyngeal and laryngeal reflexes are markedly diminished; swallowing is difficult; fluids frequently regurgitate through the nose; mastication is fatiguing. The lateral movements of the lower jaw are feeble, he cannot open the mouth widely; the tongue movements are good; lagophthalmos is present, greater on the right side; the conjunctival reflexes are diminished; the pupils react well; the neck muscles, sterno-mastoids, and trapezii are weak.

The patient cannot lift his hands up to the horizontal. The respiratory excursions are feeble. He does not complain of dyspnœa. The legs are feeble. The deep reflexes increased. There is no ankle clonus and no atrophy or fibrillary twitchings, while the electrical excitability of the muscles is normal. There is no affection of bladder, rectum or sensation.

January 9, 1892.—The abdominal muscles are feeble. The knee-jerks are poor and more difficult to elicit the longer one tries.

January 25.—The patient feels weakest after sleep, after a few movements he is better. In blowing the nose air comes through the mouth.

February 8.—The knee-jerks become feebler the longer the tendon is struck, that on the right side finally disappearing.

February 10.—It is especially the large muscles near the trunk which are affected. Tiring of the extremities diminishes the power in the others.

January 4, 1893.—He remains now practically well.

Treatment.—Galvanic stream to the spinal cord. Potassium iodide, iron and arsenic internally.

Case 17, Goldflam (13).—A male, aged 25, was seen in April, 1892. Ten years ago he had typhoid, which lasted three months. A mental affection followed. He refused to take food, was morbidly shy and tried to commit suicide. The present illness began four months ago, without observable cause, with weakness in the arms and legs. These symptoms developed in the course of two weeks. Shortly after he had difficulty in chewing. The neck muscles became affected, and giddiness developed. A month ago he had a very bad attack of dyspnœa and general loss of power of movement.

State.—A well-developed man. There is paresis of the lower face; he cannot whistle. He can shut the eyes well; the tongue and palate act normally. Chewing is difficult. There are no psychical disturbances; patient is, however, anxious about his condition. The neck muscles are feeble; the deltoid and upper arm muscles are most affected, while in the lower extremities the flexors and extensors of the hip are chiefly involved. The tiring of one extremity appears to have no influence upon the others. The deep reflexes are increased; there is slight ankle-clonus. The muscles all react normally to electricity. The symptoms vary from day to day.

July 1.—The deep reflexes are somewhat difficult to obtain.

March 16, 1893.—The patient is now almost well. He has had two relapses, both brought on by a fright.

May, 1894.—The patient only remained well for six months; the symptoms are again present.

Case 18, Goldflam (13).—Governess, aged 22, was seen on April 13, 1892. With the exception of anæmia and headache, especially during the last winter, she has always been healthy. The present trouble began three weeks ago without discoverable cause, with headache, photophobia, trembling in the eyelids, and diplopia. A week later she had a feeling of oppression, then of weakness and heaviness in arms and legs; later still, right-sided ptosis and difficulty in chewing, the jaw tended to fall down and had to be supported by the hand. Fluids came through the nose. The voice became nasal. There were no signs of hysteria. The patient's father died of a brain tumour; her mother had a congenital divergent strabismus.

State.—A fairly well-developed, rather pale girl; internal organs normal; pulse 90. Except for the right-sided ptosis, the eyes are normal. There is lower facial weakness and paresis of the palate, its reflex excitability being diminished. The tongue is somewhat thin, but its mobility is normal. Speech nasal, and chewing difficult. The movements of the head are weak. The head tends to fall forward. The deltoid appears to be the weakest muscle of the arms. There is very little weakness in the lower extremities. The electrical excitability of the muscles is normal. The deep reflexes are very active. She suffers from attacks of dyspnœa.

May 2.—Swallowing is difficult.

September 20.—She is much better; the nasal voice is still present, but no other symptoms of the disease.

Case 19, Dreschfeld (14).—A widow, aged 36. Fifteen years ago she developed sudden double ptosis, but completely recovered in six months. Ten years ago she had a second attack of ptosis with diplopia, followed by difficulty in speaking and swallowing, and weakness in the arms; she had to stop eating frequently because her jaws ached; she could not properly open her mouth to protrude the tongue, and she lost the power of whistling. The eye symptoms improved, but about nine months afterwards she suddenly became worse and was admitted.

On admission.—The intrinsic ocular muscles are normal; she has ptosis, and the extrinsic muscles supplied by third nerves are nearly completely paralysed; while the fourth and sixth on both sides are completely paralysed; the masseters, pterygoids and temporals are much weakened; she cannot close the eyes,

wrinkle the forehead, or frown, press the lips together, smile or whistle.

The movements of the tongue are very limited, it is somewhat atrophied; the depressors of the hyoid are weak; the soft palate is paralysed, there is no palatal reflex; there is difficulty of swallowing; great difficulty in clearing fauces and posterior nares of saliva and mucus. Difficulty in articulation; the laryngeal abductors are weak; the sterno-mastoids and trapezii are somewhat atrophied; the diaphragm acts slightly; the deltoids are atrophied and paralysed; there are no fibrillary twitchings; pulse 130; the wrist and triceps reflexes are markedly increased. The facial muscles show no reaction of degeneration.

November 22.—The patient is much worse; she is markedly cyanosed, the respirations are spasmodic and dyspnœa is great; swallowing is impossible, and there is no longer true articulation; the patient can only produce a faint grunt. The pulse is at times intermittent, weak and thread-like. During the night the breathing became much more laboured, the temperature rose to 99·5, and the patient gradually sank and died.

Post mortem.—Careful microscopic examination revealed nothing. The muscles were not microscopically examined.

Case 20, Suckling (15).—A barmaid, aged 21, complained of great general weakness. A brother has epilepsy, a sister paralysis. The patient's illness commenced three years ago with weakness in the arms and later in the legs. She attributes her illness to overwork. Eighteen months ago, while singing, her tongue became paralysed and she could not articulate distinctly. Twelve months ago she had difficulty in swallowing and liquids came down her nose. Five months ago she began to have suffocative attacks. There is no history of diphtheria.

State.—There is slight double ptosis, the eye movements are sluggish and restricted in all directions, especially upwards. The right eye cannot be turned up at all and forced movements in any direction are attended with nystagmus; diplopia is present at times, the pupils and discs are normal. She could not close her eyes tightly and fibrillary tremor of the ocularis muscle occurred when she tried to do so. The tongue is weak, and speech indistinct. There is difficulty in swallowing; no paralysis of the soft palate could be discovered. The palatal reflex is present; mastication is impaired. The arms cannot be lifted from the shoulders, the deltoids are large and all the other muscles normally developed; there are no sensory changes, no

exaggeration of the reflexes and no electrical changes. The spinal muscles are weak, she is unable to sit up; when lying down she cannot get up at all without assistance; the legs are very weak, she cannot lift them off the bed. The gait is slightly waddling, and she would fall if not supported. The knee-jerks are a little increased, no ankle clonus, plantars absent. There are no sensory changes. The feet and hands are blue. The patient cannot lie down in bed, as she dreads an attack of suffocation. An attempt to examine the throat brings on inspiratory stridor and cyanosis to such an extent that the patient seems to suffocate. There are no hysterical symptoms. She remained under observation three months, when she was *in statu quo*.

Case 21, Suckling (15).—A female, aged 18, with a neurotic family history. Her illness is attributed to exhaustion, and commenced gradually three years ago. She is unable to walk more than a hundred yards without becoming exhausted. The arms are weak and the grasp feeble. She cannot hold her arms out or place them on her head. There is slight ptosis, squinting, and diplopia at times. The movements of the eyeballs are restricted in all directions. Nystagmus is present. The knee reflexes are a little increased, there is no ankle clonus. There are no electrical changes. She complains of difficulty in swallowing and mastication. After mastication the jaw drops, she has difficulty in articulation. She is slightly choreic, has no suffocative attacks, and there are no hysterical symptoms.

Case 22, Wernicke (16).—A female, aged 16, admitted June 16, 1893, with the following symptoms: Ophthalmoplegia externa, incomplete double ptosis, bilateral facial weakness, upper and lower. Paresis of motor fifth and of muscles of deglutition; only fluids can be swallowed and they occasionally come through the nose. No affection of the tongue or speech. Paresis to a marked degree of both neck and shoulder muscles. Upper arm, forearm and hand weak, but she can use them still. Thigh muscles slightly stiff, otherwise the legs are not affected. Her illness developed gradually four months ago with slight temporal headache. The electrical excitability of the muscles is intact although in a few muscles quantitatively slightly diminished. The tetanic induction stream produces instead of a lasting only a temporary muscular contraction. The doubtful diagnosis was amyotrophic lateral sclerosis with bulbar complications.

July 17, 1893.—She was admitted to Clinik of Professor

Mendel. She now has palate, tongue and jaw weakness, and anæsthesia of the pharynx and larynx.

Sixteen days after admission the patient died suddenly of asphyxia. The autopsy was negative, the only change being considerable vascular dilatation, particularly in the Hirnstan, and numerous recent hæmorrhages.

Case 23, Mayer (18).—A patient suffering from difficulty in speaking and swallowing, weakness of the jaws, bilateral ptosis, paresis of extremities, and abnormal fatigability; the symptoms were worse towards evening and after exertion. There was no atrophy and no disturbance of the reflexes. Temporary improvement was followed by sudden death by choking.

Post mortem.—It was found that the cells of the hypoglossal nucleus, with the exception of a small number which were vascuolated, were completely normal, as were the cells of the anterior horns and pyramidal tracts. On the contrary, there was a marked pathological change in the intra-medullary portion of the anterior roots, also in the hypoglossal root, particularly distinctly seen in Marchi preparations, such preparations showing all along the anterior roots, as also in places on the hypoglossal root, stripes and flakes of dark myelin. The intra-medullary parts of the anterior roots, as well as of the hypoglossal root, appear distinctly atrophic, when the nerve sheath stain (Markscheiden färbung) is used.

Case 24, Strümpell (24).—A female, a field-worker by occupation, aged 21. Admitted December 30, 1893. Ten months ago she began to have difficulty in speaking and in raising the upper eyelids; six months ago she noticed weakness in the arms after working in the fields, and in the legs after walking, also difficulty in swallowing and chewing, and double vision.

Present state.—There are bilateral ptosis, weakness of the face and jaw muscles, and weakness of the extremities without atrophy. Speech is indistinct, the letters *b*, *d*, *g*, *j*, *m*, *n*, *s*, are especially badly pronounced. Sensation and the sphincters are normal; the reflexes are normal and could not be exhausted, although after repeated tapping the knee-jerks seem to diminish slightly in activity, great exhaustion is rapidly produced and amounts to almost complete paralysis of nearly all the muscles. She was worse at the menstrual periods. From January, 1894, until she died she had almost daily severe attacks, during which, if walking, she would fall suddenly to the ground, become cyanosed and breathless. Respiration became noisy, sputum accumulated in the mouth,

she could neither spit it out nor swallow it; the tongue sank back; if in bed she would sit up with her head bent forwards, saliva flowing out of the mouth. The arms when raised fell flaccid by her side, the extremities were cold. She developed a catarrhal pneumonia, and died suddenly during one of these attacks.

A *post mortem* was made, the medullary nuclei being particularly examined, and no changes were found.

Case 25, Murri (25).—A patient suffering from severe bulbar symptoms, characterised by a tendency to improvement. The disease has lasted for ten years; the myasthenic reaction is present, and the early exhaustion after exercise. In this case, even when complete exhaustion was produced in the muscle by an undue current, the muscle can be readily contracted, voluntarily (and the reverse).

Case 26, Charcot and Marinesco (22).—A boy, aged 13, suffering from complete ophthalmoplegia externa, complete paralysis of the lower, incomplete of the upper, extremities, trunk and face. Death occurred after three months with bulbar phenomena. The symptoms developed in the order above mentioned. There is no affection of sensation nor of the sphincters, and no mental change. There is no affection of the internal organs except an enlargement of the thyroid gland. There are no qualitative electrical changes, but in some muscles there is diminished excitability both to the galvanic and faradic currents.

Post mortem.—Some recent hæmorrhages were found beside the aqueduct of Sylvius, and some others, but less pronounced, at the level of the ventral nucleus of the vagus. No other changes were met with in the central or peripheral nervous systems.

Case 27, Pineles (23).—A male, aged 25. No ætiological factors were discoverable. The onset of the disease was sudden, with headache, giddiness, diplopia, and right-sided ptosis.

In July, 1893, he had difficulty in chewing and swallowing, nasal and indistinct speech, weakness in the arms and legs, and attacks of dyspnœa and palpitation. All these symptoms developed within a few weeks, and were most marked towards evening. The mental state and sensation were normal; there were no hysterical stigmata. There were no electrical changes and no atrophy. The knee-jerks were somewhat active; the palate reflex was present.

Pineles records two other cases which ended fatally after one and a half and two years respectively, death being due in each case to an attack of dyspnœa.

Case 28, Collins (26).—A woman, aged 27, the mother of two healthy children. Three years ago, when six months pregnant, she complained of weakness of the extremities, and soon after left-sided ptosis and diplopia developed, the ptosis disappearing after two or three months. Ptosis of the other eye then appeared, lasting for two months. Following this there developed difficulty in articulating, fatigue on chewing food with difficulty in swallowing and in moving the tongue, with almost complete inability to move the extremities. On first attempting to talk speech is fairly distinct, but soon the tongue becomes heavy, the lips unwieldy, the voice hoarse, weak and nasal. Fluids regurgitate through the nose on swallowing. The weakness is sometimes greatest in the extremities, at others in the muscles supplied by the cranial nerves. The intrinsic muscles of the eye are normal. Attacks of distressing tachycardia and paroxysmal dyspnœa occurred.

These symptoms improved, but she relapsed three months ago. She wakened one morning with paralysis of one side of the face which lasted three days. Since then gradual improvement has occurred. She can now walk provided she does not overtax her strength. She cannot tightly squeeze her eyelids together, she cannot hold her lips firmly together, the tongue is weak (not atrophic), the voice nasal, labials are imperfectly pronounced; the arms easily tire.

The reflexes at first appear normal, but after striking the patellar tendon several times the response gets less and less, finally ceasing to reappear after rest. There is no reaction of degeneration. The electrical responses are normal. There are no fibrillary twitchings.

Case 29, Fajersztajn (27).—A man, aged 23, was seen in April, 1895. He was said to have caught cold ten days previously. This led to great weakness in the legs and difficulty in chewing, swallowing and speaking.

Present condition.—Slight ptosis. The patient tries to prevent this by over-action of the occipito-frontalis. Blinking does not occur often; there is slight lateral nystagmus on looking to the lateral extremes, the orbicularis palpebrarum is weak, especially after frequent closing of the eyes. He can whistle for a few seconds; he can only blow out light two or three times; occasional slight fibrillary twitching of mentalis occurs; the tongue easily gets tired; the pharyngeal reflex present; there is decided weakness of the masticatory muscles increasing with their use. Biting crusts causes great fatigue. There is difficulty in swallowing; the cervical muscles are weak, but the head is held

erect. Speech is nasal, weak and rough, and becomes more nasal and weaker when continued; after counting forty to fifty slowly, he becomes aphonic. The breathing is chiefly diaphragmatic and is quickened by the slightest effort; there is decided weakness of the trunk muscles, and he cannot raise himself into the sitting posture while in bed without using his arms; he can only lift his arm over his head ten to fifteen times, even lifting a spoon to his mouth soon tires him; he can write twenty to thirty letters with a steady certain hand, when the writing becomes irregular and soon impossible. There is similar weakness in the lower extremities; he is obliged to rest after walking a few paces. The plantar, cremasteric and abdominal reflexes are normal; the tendon-jerks and electrical reactions are normal.

After six months' rest in bed and administration of strychnine, improvement in all the symptoms followed; afterwards at times there were transient relapses The symptoms were always worst towards the end of the day.

Case 30, Silbermark (28).—A male, a cook, aged 34, entered Nothnagel's Clinik, June, 1896; his family history and previous health were satisfactory. In December, 1894, he found when rolling dough that the third and fourth fingers were weak and tended to drop. After a short improvement, weakness and a feeling of fatigue appeared in the upper limbs, a few months later in the lower. Difficulty in chewing, and regurgitation through the nose appeared, together with facial weakness, difficulty in swallowing and nasal speech. Great variations occurred in the intensity of the symptoms. He always felt better in dry, warm weather than when it was cold and damp.

State.—June 5, 1896. A slight degree of ptosis is present. The ocular movements are free; von Graefe's symptom is present; the pupils react well. There is no weakness of the jaw muscles. The facial weakness is most marked on the left side. There is no weakness of neck; the limbs are affected. Tiring of one hand had no effect on the other.

Case 31, Devie et Roux (29).—An unmarried woman, aged 43, entered hospital July 3, 1894. The symptoms gradually developed two to three months ago without any affection of her general health. She has almost complete paralysis of the extensors and rotators of the head and neck: the head falls forwards, the chin touching the chest; she can only with great difficulty lift the head without using her hands. The rotators

are somewhat less affected. Beyond slight paralysis of the right inferior facial there are no bulbar symptoms. Bilateral ptosis is present, very marked on the left, much less on right side; the globes are practically immobile; the orbicularis palpebrarum is intact; the reflexes are normal; fundus: there is slight perivascular œdema of the optic discs, the margins being indistinct. Potassium iodide and mercury were used.

July 16.—The cervical muscles are less paralysed, also the ocular muscles, but the ptosis remains unaltered. Specific treatment steadily pushed.

August 10.—There is steady improvement, and greatly increased power in the cervical muscles. The muscles of eyeball are almost normal; the ptosis is very slight in the morning, but gets marked by mid-day.

August 20.—Movements of the head are normal, the ocular movements almost so. The ptosis is confined to the left eye and this only towards the end of the day; there is slight nystagmus. The mercury was stopped, iodide continued.

September 16.—Left the hospital practically well.

December.—Re-admitted for observation. Iodide has been continued. She has slight and transitory ptosis, but no other symptoms are observed. Discharged May, 1895.

July 31, 1895.—The patient was seen on this date, practically well.

November 20.—Third admission. Ptosis for two months reappeared on the left side, with slight diplopia, most marked towards the end of the day. Except for slight paralysis of right face, there are no other symptoms. There is no atrophy of the cervical muscles.

Case 32, Kojewnikov (30).—A male, aged 54, who had previously been healthy. There is no history of syphilis or alcoholic excess. The disease began suddenly some hours after a severe chill, when he first noticed weakness of the lips. Soon after he had a feeling of tightness of the face, difficulty in closing the eyes, in chewing, in swallowing, and nasal speech.

State.—The patient suffers at present from leftsided ptosis, weakness both of the upper and lower face, at times diplopia, limitation of the tongue movements, difficulty in swallowing (he had to be fed with a tube). He becomes easily tired when speaking, breathing is laboured, the face muscles are manifestly atrophied, both masseters, particularly the left, being very atrophic. The skin and deep reflexes are normal and there is no affection of sensation or of the special senses. At first he

became worse, then he improved. Six months later after a chill the symptoms returned. There was then a slight difference between the pupils and slight insufficiency of the left internal rectus. The mouth was usually held half open and there was great tiredness of the muscles in chewing, speaking and swallowing. There were no electrical changes. The patient died suddenly, probably from paralysis of respiration, two and a half years after the onset of the disease. There was no autopsy.

Case 33, Kojewnikov (30).—A female, aged 17. No history of syphilis or alcohol. A brother has spasmodic asthma. Since the onset of menstruation in 1889 her health has been indifferent. Her present illness seems to have dated from this. She first noticed a difficulty in utterance and nasal voice. This continued till February, 1890, when she could neither whistle, blow out a candle nor expectorate, and was suffering from ptosis and difficulty of swallowing.

September, 1894.—There is weakness of the facial muscles, especially the lips; the lower lip falls. Speech is difficult and easily tires; the voice is nasal; there is left-sided ptosis. There is slight symmetrical wasting of the tongue. The soft palate is immobile. The muscles of the shoulder and hip are weak. Sensibility and the tendon reflexes are normal.

Summer, 1895.—There is defective taste and occasional diplopia.

September.—She is much worse; there is weakness of the extremities, an inclination inwards of both eyes, and difficulty in holding the head up—it falls forwards.

October.—Speech is worse, swallowing impossible.

October 14.—The right pupil is slightly the larger, she cannot firmly close the eyes; mastication is very difficult. There is no atrophy of facial or masticatory muscles, but distinct atrophy of the tongue. The soft palate is almost immobile; defective adduction of the cords is seen on phonation; the posterior cervical muscles are weak and somewhat atrophied.

Electrical reaction; facial muscles show slight quantitative diminution to electrical currents. The soft palate does not respond to either current. In the tongue muscles A.C.C. is slightly better than K.C.C.

There is a distinct trace of sugar in urine; the patient has not menstruated since April.

Sensation is normal. She can only taste salt, and that imperfectly.

She is low spirited and very irritable.

The gravity of the symptoms varies, the muscular weakness being least marked in the morning.

October 26.—An attack of dyspnœa occurred during sleep at night, she was unconscious and cyanosed; it lasted three hours. She has had similar slighter attacks since.

November 1.—She improved from this date; sugar permanently disappeared from the urine on November 13.

December.—*In statu quo.*

In April, 1896, she left the hospital, still complaining of the chief symptoms.

Case 34, Toby Cohn (31).—A girl, aged 19, who has been ill for a year with weakness and tiredness in the arms and legs, ptosis, difficulty in swallowing, regurgitation of fluids through the nose, and nasal speech. All her symptoms are more marked towards evening.

On examination she was found to have double ptosis and lagophthalmos on both sides, a fixed expression with facial weakness on both sides; the jaw movements are feeble, the palate easily tired, speech is often nasal and difficult to understand, the letters *g* and *k* being especially difficult to pronounce. The tongue is normal, the neck muscles easily fatigued. The arms too are easily tired, and cannot be raised so well when sitting as when standing or lying. A similar condition of the lower extremities exists; after walking for some time a waddling gait develops as in the dystrophies. The knee-jerks are pretty lively. A paresis of the abdominal muscles exists. There is no ataxy, and sensibility is everywhere normal. The myasthenic reaction is very distinct; there are no other electrical changes. The internal organs are sound, the urine healthy, and there is no mental change. The family history is good; she had no preceding illnesses. An abnormal increase of the leucocytes is present in normal proportions.

Case 35, Kalischer (32).—A male, aged 64. No history of syphilis or alcohol. He had small-pox forty years ago, but otherwise his health has been good. In September, 1892, he developed double ptosis, paralysis of the extrinsic ocular muscles, and a week or two later paresis of all four extremities. A flaccid paralysis. The deep reflexes are increased, the skin reflexes lost; there is no atrophy or fibrillary tremor; the extensors are weaker than the flexors. There is no reaction of degeneration, but some diminution of faradic excitability in muscles and nerves.

There is no sensory disturbance, no sphincter trouble. The paralysis is always least in the morning. Later on the pupils

became sluggish, particularly to light. Death occurred apparently from paralysis of respiration.

Post mortem.—Microscopical examination. The changes observed in the microscopical examination were numerous old and recent hæmorrhages, some large, some small, in the whole of the cerebral gray matter from the posterior part of the third nucleus to the sacral region.

There was degeneration in the nuclei and cells of the anterior horn all through the medulla and cord, varying in degree in different parts.

The position of the lesion did not correspond with the symptoms present during life.

Case 36, Widal et Marinesco (33).—A man, aged 31. Suspected of having tuberculosis. He developed severe headache, and in a few days the typical features of asthenic bulbar paralysis—ptosis, diplopia, weakness of external eye muscles, deep monotone voice, facial and palatal paresis, difficulty in chewing and swallowing, weakness in the neck and arm muscles, and the legs were easily fatigued. Typical variations in the intensity of the symptoms occurred. Dyspnœa and a small fast pulse were present. He died suddenly fourteen days after the commencement. For the last eight days the fever was 38-39°, and there was a trace of albumen in urine.

Post mortem.—The third, sixth, seventh and twelfth nuclei and cells of anterior horns examined by Nissl showed *chromatolysis*, the vessels were widened, there were no hæmorrhages; in the roots of the third, seventh and twelfth nerves degenerated fibres were seen by the Marchi method.

Case 37, Berkeley (34).—A male, aged 28, whose family history was good. When 14 years old slowness of movements attracted attention. His sister said, "When he stooped he never seemed able to get up again." Seven years ago the symptoms of his present illness were first noticed; he was easily tired and rather somnolent; he had an inordinate appetite. Four years ago he was troubled with vomiting after meals, which lasted for three or four months. Soon after he developed pronounced *deafness*, which persisted for several months, and has never entirely disappeared. His gait was clumsy and he was apathetic. Articulation was difficult and gradually became worse. A year ago the eyeballs became "stiff," and double ptosis with a peculiar facial expression appeared. There was no history of syphilis or alcoholic abuse.

State.—September, 1892. The facial expression is dull and heavy, the patient usually sits with his head bent forward because of weakness of the muscles at the back of his neck. The muscles of extremities are very feeble and easily exhausted. There is no atrophy or fibrillary twitchings. Sensation is normal; he is somewhat deaf. Bilateral anosmia is present. The pupils are semi-dilated and do not respond to light or accommodation. Deep reflexes increased, muscles react normally to faradism but are easily exhausted. Heart regular. Pulse fast (120). No albumen or sugar in urine. Incomplete double ptosis exists; the internal and inferior external rectus and oblique muscles of both eyes are paralysed. The eyes are practically immobile except that he can roll them upwards slightly. The masseters are weak and easily fatigued by faradism. There is weakness of the face muscles, the forehead is smooth, the orbicularis responds feebly, whistling is impossible, all the letters of the alphabet badly enunciated, the palate hangs low, the pharyngeal and palatal reflexes are well marked; no laryngeal examination was made. The tongue movements are defective. Contented disposition. Duration of illness ten years.

July 13, 1895.—While being fed with soup he *suddenly* choked and *died from asphyxia*; he had had no previous attack of dyspnœa.

Post mortem.—An old hæmorrhage was found in corpus callosum, having occurred probably in early life, perhaps when he had variola, aged 18 months.

This might account for the cerebral condition. No changes were present in the nuclei of medulla or pons, either in the cells or vessels; particular attention paid to third nucleus, but nothing abnormal found.

Case 38, Schlesinger (35). (*Very doubtful case.*)—A female, aged 29, admitted August 12, 1894, had had good health. Six weeks previously she became suddenly ill and experienced great difficulty in swallowing. Fluids especially were difficult to swallow, regurgitation through the nose took place, and there was a copious secretion of saliva which frequently flowed out of her mouth. There was frequent vomiting. After a few days she was better, but the arms and legs began to feel weak. Her condition gradually got worse.

State.—August 19, 1894. The mental state is normal, speech is slow and hesitating, the pupils are equal and react promptly. The eye movements are free, there is no diplopia, and no affection of the face, tongue, or larynx.

A high degree of general muscular atrophy is present. The

muscles in shoulder region on both sides are both fairly markedly atrophied, particularly the posterior part of deltoid.

There is marked atrophy of the thenar and hypothenar eminences.

The arm-jerks on the right side are absent, on the left side they are very feeble. The muscles of lower extremities are much atrophied, but react to faradism. The knee-jerks are obtainable, but not increased, and sensation is completely normal except a large patch corresponding to the deltoid and right side muscles, where the sense of temperature is lost. There is retention of urine, requiring the catheter, and obstinate constipation.

Towards the end of August she became worse, vomiting and difficulty in swallowing developed, with increased salivation and rapid pulse. Tongue deviated to the left; the larynx was normal.

September 18.—Died from paralysis of the diaphragm.

Post mortem.—Nothing abnormal found; Weigert-Pal, Nissl, and Marchi all being used.

Case 39, Brissaud et Lantzenberg (36). (*Doubtful case.*)—A carpenter, aged 41, who had had bronchitis and pleurisy, noticed great general wasting after a cardiac illness (? myocarditis). One and three quarter years after the onset he had right facial weakness with inability to open the eyes to the full extent, a wasted, powerless tongue, double vision and weakness of the external eye muscles. Atrophy and weakness of sterno-mastoid and neck muscles, also in the arms and legs, with occasional fibrillary twitchings. Diminished knee-jerks, rough nasal speech and dry cough. Six months later there was a distinct improvement in most of his symptoms, except the fatigability of the muscles. No affection of swallowing. The jaw muscles, which were weak, now act well. No myasthenic reaction. Progressive improvement occurred. No statements as to ultimate result.

Case 40, Karplus (37).—A female, aged 24. Healthy family. When 5 years old she developed slight right-sided ptosis, which progressed. The following week the left lid was also affected. After a year the ptosis gradually disappeared. Since then every year for periods of several weeks ptosis has appeared, worse towards evening. There was occasional diplopia.

November, 1894.—She had ptosis, paralysis of the external eye muscles, weakness and tiredness of the upper and lower extremities.

December, 1894.—Paralysis of the external eye muscles. Paresis of the frontalis and ocularis; weakness in mastication.

After two months the weakness of the extremities disappeared and the ocular movements improved.

Autumn, 1896.—No ptosis; weakness of superior and inferior recti is present.

Case 41, Eulenberg (38).—A man, aged 28. Family history satisfactory. He had inflammation of the throat with a diphtheritic-like membrane a few months before onset of present illness; no syphilis; no excessive alcohol or tobacco history. In December, 1894, he saw double, and complete right-sided ptosis developed suddenly; later ptosis developed on the left side. In February, 1895, these symptoms disappeared, to reappear again gradually in November of 1895. From the middle of 1896 to the middle of 1897, he was again quite well. Since June, 1897, he has suffered from irregular cardiac action, ophthalmoplegia developed, and weakness of both arms and legs, especially on the right side.

State.—December 6, 1897. Complete ophthalmoplegia externa on both sides, the muscles are not all affected to the same degree. The right pupil is dilated and its reactions are sluggish; the papilla is of a whitish colour, but there is no disturbance of function (later the dilated pupils scarcely reacted at all to light); on the left side the optic nerve was hyperæmic; double facial weakness, particularly of the orbicularis palpebrarum muscle; movements of the jaw and palate are weak and deglutition is difficult; on the left side his ability to hear deep tones is diminished (insufficiency of the tensor tympani?). There is weakness of the trunk and limb muscles which varies from time to time. There is striking increase of the muscular sensibility (*auffallende steigerung der muskelsensibilität*) in the limbs for electricity, especially for faradic currents. The myasthenic reaction is present in the extensors of the left forearm, the right extensor indices, and markedly in the interossei of the right side. Great improvement occurs after prolonged rest. There is no muscular atrophy; the reflexes are preserved; sensibility is intact.

Case 42, Mailhouse (39).—A male, aged $2\frac{3}{4}$ years. He has suffered greatly from the heat. A week ago he had a mild attack of diarrhœa a few days prior to the onset of the first symptoms.

July 6.—The child could not hold up its head properly, at other times the head was as erect as usual. There was no fever or vomiting, and no complaint of pain. He was unable to chew or to swallow properly, fluids tended to regurgitate through the nose. At times speech was affected so that he could not be clearly understood, at other times it was natural. He has not been con-

fined to bed. The parents noticed that his eyes were half closed and that he could not smile. The family history was good.

State.—Marked bilateral ptosis, pupils and external eye muscles normal.

The face is expressionless, he does not smile, saliva runs out of the mouth. The mouth is half open, the soft palate normal, and the voice good. The reflexes are normal. After walking a short way he becomes unsteady on his legs, so that he asks to lie down. There is no atrophy. The electrical examination was unsatisfactory owing to uneasiness of child. The pulse 84; temperature normal. He was ordered to rest in bed and given strychnine and an intestinal antiseptic.

July 19.—Mailhouse was sent for because of peculiar rolling of the eyes; his mother thought he was weaker.

July 31.—Ptosis is gone; there is no strabismus; he can chew, swallow and smile, and runs about as he did before he was taken ill.

August 4 (*evening*).—A choking attack occurred during an attempt to swallow; weakness of neck muscles and regurgitation of liquids, &c., followed. He was better by the time the doctor got there.

August 5.—He has been up and down during day. While attempting to drink coffee from a cup a little difficulty in swallowing was noticed, his head drooped and he was dead.

He never had any attacks of dyspnœa; the heart's action was good.

There was no autopsy.

Case 43, Laquer (40).—A female, aged 21, whose mother died of phthisis. She had suffered previously from anæmia. She developed right-sided ptosis and double vision, and later difficulty in swallowing and regurgitation through the nose; ptyalism was present. Speech became indistinct and nasal; the arms and legs became weak. Three months before she had given birth to a child.

State on examination.—Left facial paresis; left-sided ptosis; weakness of the left internal and right external rectus, and diplopia; difficulty in whistling; speech slow, very indistinct and nasal in character; larynx normal. Tenderness on pressure over the fifth nerve on both sides. The knee-jerks were increased; there was shortness of breath. Great weakness in arms and legs was present, and often great difficulty in swallowing. The symptoms varied in intensity. The patient died suddenly one and a half years after the onset of her illness. The autopsy was negative, but there was no microscopic examination.

Case 44, Laquer (40).—A male, aged 49. Family history good. He has had pneumonia and repeated attacks of gout. He complained of pain and weakness in the right arm and leg; later, weakness in both arms. Double vision, ptosis, tiredness of the eye, face, and jaw muscles appeared; also of arms and legs. Fatigue of one group of muscles produced exhaustion in others, the myasthenic reaction was demonstrated in the biceps; there was no atrophy or bladder trouble, while sensation and the reflexes were normal. After an attack of bronchitis all the symptoms became intensified. His expression was that of a man falling asleep after the mid-day meal. Chewing, swallowing, and speech all showed early signs of fatigue. After glancing outwards and inwards several times the eyeball became fixed. There was no laryngeal affection.

Six months after its onset all the symptoms of the disease became much more pronounced. Distinct atrophy of the deltoid, biceps, triceps, pectorals, interossei, quadriceps, and calf muscles, developed. The tendon reflexes were brisk and could not be tired out. The myasthenic reaction was present. Some muscles, especially the gastrocnemii and extensors of the forearm, are tender on pressure.

Case 45, Wheaton (41).—Governess, aged 33, who had always been nervous. There was no neuropathic heredity. She had worked very hard. About the second week in July, 1896, she had a tooth extracted; the dentist told her that she must be very careful, or her gums would start to bleed and she might bleed to death. This frightened and worried her greatly. On July 21 she had a severe headache, in the morning she could raise the eyelids only with difficulty and the light pained her. On July 22, excepting for these signs and in addition ptosis and a slight increase of the reflexes, nothing abnormal was noted. During the next few days the ptosis became more marked, there was difficulty in chewing and in keeping the mouth closed. She was unable to sleep and had occasional attacks of palpitation. All the symptoms were increased by exertion.

August 14.—She had difficulty in walking, the muscles of the the neck were weak, menstruation began, and all symptoms increased in severity. She had difficulty in swallowing.

August 31.—She had a severe choking spell.

September 7.—To-day the patient had a bad spell of difficulty in breathing.

September 14.—She died in an attack of dyspnœa.

Mentally somewhat despondent. The reflexes increased

gradually during the disease; there was no atrophy of the tongue and no tremors. The pulse was usually between 90 and 110.

There was no autopsy.

Case 46, Saenger (43).—A female, aged 22, seen December 29, 1896. She has been married one and a half years but has no children. Her previous health was good. Four weeks ago, she suffered from headache and sore throat. Difficulty in swallowing and double vision followed. Eye disturbance was present before the sore throat. The patient is anæmic and has a fixed facial expression. She has difficulty in preventing the upper lids from drooping. The eyes cannot be moved either inwards or outwards. The pupils are equal and react normally; she has difficulty in swallowing. The palate is weak. The voice is feeble. The pulse is somewhat rapid and regular. There is great diminution of power in both the upper and lower extremities; the gait is normal, but walking soon makes her tired. Now and again there is weakness of the neck muscles; the symptoms are more intense towards evening. Sensibility and the reflexes are intact; neither the myasthenic reaction nor reaction of degeneration are present.

January 1, 1897.—The patient is somewhat better, she still has pain in the spine and nape of the neck.

January 10.—She walks better.

January 13.—There is marked diplopia.

Subsequently she became pregnant and got practically well of the paralysis.

Case 47, Montesano (45).—A shoemaker, aged 17. Fourteen days after a cold bath, which he took when overheated, he was affected with weakness in the legs, so that walking was soon impossible; then fatigue appeared in the arms and trunk, and diplopia. The spleen was slightly enlarged. The muscles were very easily fatigued. There was inability to dorsiflex the hand, and to extend the fingers, deviation of the tongue toward the left and weakness of the left side of the face. The superior oblique and the external rectus of the left eye were paralysed. There is no affection of sensation. The faradic excitability of the muscles of the left half of tongue and right hypothenar eminence is diminished.

The myasthenic reaction is present in the lower extremities, especially in the quadriceps. Voluntary movement is still possible after exhaustion by faradism.

After four months the patient had recovered, excepting for slight diplopia and slight weakness in the finger movements.

The author suggests an organismal origin for the disease, the organisms becoming virulent in consequence of the above-mentioned chill.

Case 48, Kostetzki (47).—A male, aged 24, who had suffered from attacks of palpitation and dyspnœa, developed weakness in his trunk and extremities, so that he had to give up work. The voice became nasal, the breathing was uneasy. The symptoms gradually disappeared after a few weeks. Two months later, after a severe mental shock, difficulty in swallowing developed.

Present state.—The patient is very thin, his muscularity is feeble. There is bilateral ptosis, and the expression is mask-like. The muscles of the face are paretic. Movements are scarcely noticeable. The tongue can only be protruded very slightly. The pharynx and larynx muscles are paretic. Speech is indistinct and nasal; chewing is difficult, and he has difficulty in swallowing and breathing. There is paresis of diaphragm. Attacks of palpitation occur. Paresis and atrophy are present in various muscles of trunk and limbs—the pectoral, deltoids, thenar and hypothenar muscles, glutei and spinal muscles. The reflexes and sensibility are unaffected. The muscles are quickly fatigued (for example, diplopia develops after a few movements of the eyes). Improvement occurred after several weeks' treatment; a relapse then followed, and this variation in the symptoms recurred several times.

The author is of opinion that this case forms a transition variety between chronic bulbar paralysis and the so-called asthenic bulbar paralysis.

Case 49, Angelini (49). (*Doubtful case.*)—A man, aged 42, who had been nervous from youth. The illness commenced after emotional excitement, with tiredness of the muscles of the eye, the limbs and jaws. He also became soon fatigued after writing, speaking or reading, so that after a few words he could not remember what he had said. He had a severe feeling of pressure over the head and a feeling of stupor. After a short pause he could go on with his business. Sensation and the reflexes were normal. The myasthenic reaction was not present. Under hydrotherapy and strychnine the symptoms disappeared. Two years later there was a slight relapse from which he soon recovered.

The clinical picture shows an undoubted resemblance to myasthenia gravis. But while in this disease the symptoms are confined to the motor apparatus, in the case above described the higher functions were affected.

The case is more probably one of hysteria than myasthenia gravis (Angelini).

Case 50, Harry Campbell (53).—A governess, aged 28. Seen December, 1898. Twelve months ago she noticed she could sing in the morning but not at night, and since then she has gradually developed the symptoms she now complains of, *i.e.*, difficulty in swallowing; sometimes solids "stick in the throat," and fluids pass through the nose; nasal speech; a tired feeling at the back of the tongue. She cannot whistle, nor empty a spoon with the upper lip. There is upper facial weakness, but the corrugator supercilii acts well; great weakness of the orbiculares palpebrarum; after eating for some time the food tends to accumulate between the gums and teeth; mask-like expression; weakness of the face, soft palate and tongue. The above symptoms are all worse after using the affected muscles for some time. They are thus much better in the early morning than towards evening. No ptosis or diplopia. Knee-jerks and electrical reactions normal.

Later she complained of weakness in the arms, especially the right one; this she noticed in lifting her arms "to do her hair." This difficulty lasted a short time only and did not recur.

January 27, 1899.—All the symptoms much worse; she can scarcely close her eyes.

February 10.—Much better.

April 29.—Improvement continued until April 7; during last fortnight has been worse. Has had slight diplopia.

February 16, 1900.—The symptoms have fluctuated in severity since the last note was made, but the general tendency has been improvement.

Case 51, Sinkler (50).—A married woman, aged 37. Two brothers and a son suffered from nystagmus and rotatory head tremor, another son has nystagmus. There was no suspicion of syphilis. She had typhoid fever seven years ago, followed by bilateral ptosis, which lasted for four or five months. Two years ago she had diplopia. One year ago she was confined, the labour was a difficult one. A few weeks later swallowing and speaking became difficult, and weakness in the arms and legs developed. Since then at each menstrual period the symptoms have been worse.

State.—The face is mask-like, but there is no paralysis of the facial muscles. She can show her teeth and whistle. Speech is nasal and indistinct. After speaking for some time complete

aphonia results. Deglutition is difficult, sometimes regurgitation occurs through the nose; the jaws soon become tired with chewing, as do the arms and legs after exercise, the gait becoming unsteady and shuffling. The knee-jerks are present and apparently do not become exhausted on repeated testing. All the muscles respond to faradism and the faradic irritability is not exhausted. There is no affection of sensation and no headache. There is partial double ptosis, the pupils react normally, almost complete paralysis in left external rectus, and partial of the left superior rectus exist. Patient is of a cheerful disposition. The fatigue which occurs in the eyes, throat, legs and arms is very characteristic.

Case 52, Punton (51).—A married woman, aged 25. She suffered from rheumatism before marriage. She has been ill for three years. Her only child was born just previous to the first symptoms; the labour was prolonged and difficult. She has never been well since delivery.

Diplopia, dimness of vision, and left-sided ptosis were the first symptoms. Mastication, articulation, and swallowing became difficult, voice became nasal, the tongue was less dextrous and felt numb. Weariness, prostration, and rapid heart's action followed slight exertion. She became unable to whistle, and strabismus appeared in both eyes. She developed a continuous lachrymation, and lost two stones in weight.

State.—The eyeballs protrude slightly and cannot be moved in any direction. She complains of excessive lachrymation during the waking hours. Double ptosis is present, left greater than right. She has diplopia; the facial expression suggests a putty-like blankness. Profound paresis of the face, right greater than left; she cannot whistle. The masseters are equally paretic, the bite is feeble, there is no atrophy, tremor or twitchings. The tongue is thick, flabby, and completely devoid of lateral movement. The palate moves very little. Speech is thick, indistinct and nasal, and deglutition of solids difficult, while fluids regurgitate through the nose. The left vocal cord is paralysed, the power in the extremities is normal; there is no atrophy, and no twitchings or sensory symptoms; the superficial reflexes are normal, the deep are slightly exaggerated. There is no ankle clonus; electrical reactions are normal; urinary analysis negative. The pulse 90, regular.

Case 53, Clifford Allbutt (52).—A girl, aged 18. The personal and family history are good. She caught cold, followed by stiffness of the tongue and jaws, which disappeared after a few weeks.

Six months later she was seen by Clifford Allbutt. She spoke oddly, "as if with a potato in her mouth;" when she tried to read a book she began well, but soon the disorder set in and she became unintelligible. Her friends said that she read much better when at home quietly. A few weeks before she had begun to have difficulty in swallowing. "She choked over her meals, more when she was tired." There was no evidence of hysteria or of organic disease observed, except that the forefinger of the left hand seemed weak and fumbling. She moves her tongue and jaws and all the muscles of the face, throat and orbit quite normally. The palatal reflex was normal. A provisional diagnosis of hysteria was made. Under treatment she improved very much. One evening the symptoms became worse, especially the swallowing, and her mother spoke to her somewhat sharply. Next morning she went to her mother's room to protest, when she suddenly fell to the ground, was convulsed, turned blue and died. There was no autopsy.

Case 54, Seiffer (54).—A female, who has been ill eight years (age not given). The illness came on without known cause. Five years ago the fatigue in the arms and legs, which was present before, became more marked, her gait became waddling, jaw weakness and ptosis developed. The tiredness was always more marked towards evening.

State.—She has double-sided ptosis; the eye muscles act normally, but at times nystagmoid movements are present. The patient quickly becomes tired on trying to count aloud, ultimately she is quite unable to do so. She can only raise herself with difficulty from the horizontal position. The arms if held up quickly become tired, as do the legs after walking, when she wavers and ultimately staggers. There is a distinct myasthenic reaction; nothing peculiar as regards the blood is present.

Case 55, Buzzard (55).—A schoolmaster, aged 40. His paternal uncle died in a lunatic asylum, a paternal aunt died of creeping paralysis; there is no history of syphilis or alcohol. Seven years ago, after taking cold baths, the little and ring fingers of the right hand felt weak. This recurred from time to time; nasal voice, feeling of constriction in the throat and ptosis followed. During the year 1895, excepting the weakness in the right index finger, he had no trouble; legs and arms then became weak, and later there followed diplopia, weakness in the tongue and jaws, difficulty in coughing and in masticating, attacks of dyspnœa and palpitation, fatigue; cold weather and mental excitement all increase the intensity of his symptoms.

On admission.—Very intelligent man, indistinct nasal speech, diplopia, right-sided ptosis, upward movement of eyes defective, both external recti weak, pupils react perfectly, jaws easily tired, double facial weakness (especially upper face), tongue moves freely but easily exhausted, palate movements and reflex power poor. After repeated deep respirations the glottis finally opened less than at first. Great weakness of the neck muscles, arms and legs are weak, he has difficulty in dressing himself and cannot walk more than half a mile, no muscular atrophy, no fibrillary twitchings, myasthenic reaction present, no impairment of sensation, no sphincter trouble, arm-jerks poor, knee-jerks active, not exhausted by frequent tapping, nothing abnormal in the urine, other organs healthy.

While in hospital patient improved greatly, but a relapse occurred without apparent cause, the relapse characterised by the preponderance of severity of symptoms in the trunk and muscles of the extremities rather than those of the bulk.

Case 56, Buzzard (55).—A female, aged 24, housemaid. Rheumatic family history; no nervous disease. Anæmic for eighteen months, otherwise good health until a year ago. First symptom was giving way of the legs when walking upstairs, legs have been weak ever since; soon after arms became weak, speech became nasal, ptosis developed, diplopia, difficulty in mastication, in coughing and in swallowing were noticed; no attacks of dyspnœa or palpitation. When excited, symptoms are intensified; cold does not affect her; the symptoms are no worse at the menstrual period. On admission, no alteration in mental state, no affection of cranial nerves, speech almost normal at first, after reading aloud soon becomes indistinct and nasal.

Double ptosis, left pupil greater than right, ocular movements good, slight nystagmoid movements on extreme lateral deviation, convergence poor, orbicularis palpebrarum very weak, power of mastication very poor, so feeble that she cannot hurt a finger introduced into the mouth when she tries to bite it, tongue and palate movements fairly free but soon exhausted, extremities weak, no atrophy, no fibrillary tremors, myasthenic reaction demonstrated in biceps, sensation and sphincters unaffected, deep reflexes active. Knee-jerks cannot be exhausted by repeated tapping.

Case 57, Feinberg (57).—A man, aged 44, with no neuropathic heredity, developed obstinate constipation, with symptoms of obstruction, colic, meteorism and vomiting. On the fifth day he

had severe pain in occiput and region of upper dorsal spine, followed by numbness and weakness in the extremities, double ptosis, immobility of the eyeballs, feeble power of movement in the tongue and lips, inability to wrinkle the forehead, indistinct speech, continuous salivation, difficulty in chewing and swallowing, the latter only to a slight degree. The patient soon began to improve quickly.

State a month after appearance of symptoms.—A strong man. He has slight double ptosis, the ocular movements were slow, the up and down movements being defective, there was no nystagmus, the pupils react normally. The right side of the face is paretic, the left normal except for slight weakness in the left frontalis. Attempts at whistling and showing the teeth gave poor results. Speech is distinct with the exception of the labials, the tongue moves well, the power of biting is feeble on the left side. The palate moves well, the reflex is normal. There is no increase in the rate of the pulse or respiration. The occipital headache and pain in the back have long ago disappeared. All the other organs are normal; the urine contains nothing abnormal. The patient complains of great weakness and muscular prostration. There is no muscular atrophy and no disturbance of sensation. The knee-jerks are increased. There is no ankle clonus and no rigidity. He can make all movements, there is no ataxy. A feeling of tiredness is present even when he lies in bed, which is exaggerated when he stands or walks. There are no electrical changes.

Six weeks from its onset nearly all symptoms of illness had disappeared; since then he has remained well (a year).

Case 58, Leonard Guthrie (56).—Waitress, aged 23. Her previous health and family history were satisfactory.

Her illness commenced two years ago with difficulty in speaking; later, difficulty in swallowing, nasal regurgitation, inability to close the eyes and weakness in the hands appeared; all the symptoms were worse after exertion or excitement.

State.—A delicate-looking girl, but not markedly anæmic. Paresis of the orbicularis oculi and oris, tongue, soft palate, and probably of the pharynx. There is upper facial weakness but no ptosis, the ocular movements are perfect, there is no nystagmus. The pupils react well. She cannot blow out her cheeks or whistle; speech is indistinct and nasal. The vocal cords act normally. Deglutition is difficult; the jaw muscles are weak. She has fair power in the extremities, but soon becomes exhausted. Sensation and the sphincters are normal. The

myasthenic reaction is present. There is no muscular atrophy. After five weeks she was much improved.

Case 59, Raymond (59).—Woman, aged 25. Entered February 7. Dead child in October last.

January 8.—Took cold, was seized with paralysis of left infra-facial same evening, but Raymond is not certain whether the right facial escaped.

January 25.—Ptosis supervened (left); eight days ago right ptosis—this less. This paralysis is intermittent and almost disappears at times. Ptosis worse second part of day.

Towards February 7, complained a little of diplopia with difficulty in mastication. This fatigues her, has to stop every few "chews," due largely to paralysis of masseters, especially left; difficulty of protruding tongue, applying it to palate, and speech is *trainante;* labials ill pronounced; after speaking short time speech gets thick and less distinct. Intellect perfect; speech slow. Pupil reactions normal. Fundus normal. No sensory trouble. Reflexes normal. Patient complains of getting tired easily, and of not being able to walk for long.

Treatment.—Faradisation of paralysed muscles, sulphur baths and cold douches.

Improvement from February 26. April 15, cure complete.

Pflüger (gives no reference) (*Gazette des Hôp.*, 1,168), has cited a case of ophthalmoplegia externa consequent to menstrual trouble. (*De Graefe*, Landsberg, Schœler.)

Case 60, Harry Campbell (unpublished).—A girl, aged 19, who after an attack of scarlet fever three and a half years ago became paralysed all over (she could not even turn in bed). During the following year she gradually improved, and recovered power all over excepting in the face, which felt stiff. About twelve months ago she gave birth to a child. During pregnancy the face improved, but became worse again during lactation, which lasted for seven months.

On admission her chief complaint was a constant running of water from the eyes.

There is marked double facial weakness affecting both the upper and lower face; great weakness of the orbicularis oris and palpebrarum; occasional diplopia, and the eyelids often droop towards evening. There is no affection of the soft palate, tongue, or larynx, and no weakness of the extremities. The condition is worse at the menstrual periods and in cold weather. The knee-jerks are brisk; all the muscles react readily to weak faradic currents. There is no affection of sensation.

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