He cannot keep both eyes open at the same time more than one or two minutes. If he covers the left eye with his hand, the right eye stays open better, but after two or three minutes the right upper lid falls. He now can keep the left eye partially open if he covers the right eye. The weakness of the other ocular muscles seems now to be in the elevators and depressors of the right eyeball. The ocular palsy, he says, has seldom been the same at any two examinations. The deltoids react well to a rapidly interrupted faradic current, but there seems to be some exhaustion by this current in the left sternocleidomastoid muscle.

MYASTHENIA GRAVIS:

WITH SPECIAL REFERENCE TO THE OCULAR SYMPTOMS, AND A REPORT OF A CASE INVOLVING THE EYES ONLY.[1]

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MYASTHENIA gravis is rare, especially in children. Of the earlier investigators, six are pre-eminent, viz., Wilks, Erb, Oppenheim, Hoppe, Goldflam, and Jolly. The disease was first described by Wilks[2] in 1877. He recorded a case of apparent bulbar paralysis, in which death resulted in a few weeks from failure of respiration. No lesion of the medulla was found at the autopsy. In 1878 Erb[3] published three cases, in two of which the principal symptoms were bilateral ptosis, while in the third, the intrinsic muscles of the eye were also involved. Weakness of the neck muscles, paresis of the muscles of mastication and weakness of the tongue and extremities were other symptoms observed. No muscular atrophy was present. Nothing more was added to the subject until nearly ten years later, when Oppenheim,[4] in 1887, published "A Case of Chronic Progressive Bulbar Paralysis without Anatomical Findings." Shortly afterward Eisenlohr[5] reported a case in an eighteen-year-old girl, in which the prominent symptoms were ptosis and paresis of other ocular muscles. In this case, as in Oppenheim's, no lesion was found. In 1891, Goldflam[6] added four new cases to those previously reported and collected by him. In 1892 Hoppe[7] contributed an exhaustive account of the subject, signalizing a new epoch in the history of the disease. Goldflam showed that the characteristic

[1] Read before the Chicago Medical Society, November 2, 1904.
[2] Guy's Hospital Reports, 1877, vol. xxii.
[3] Ueber Einen Neuen, wahrscheinlich bulbären Symptomenkomplex, Arch. f. Psych., Bd. ix.
[4] Virchow's Archiv, Bd. cviii.
[5] Neurol. Centralbl., 1887, Bd. vi.
[6] Ibid., 1891, Bd. x.
[7] Berl. klin. Woch., 1892, Bd. xxix.

muscular symptoms—fluctuating in intensity, improving by rest and becoming aggravated by fatigue and exertion—were an abnormal tiring rather than an absolute paresis. As an addition to the clinical picture Jolly,[1] in 1895, described the peculiar electric reaction of the nerves and muscles known as the "myasthenic reaction"—*i. e.*, the muscles and nerves reacting normally to electricity are rapidly exhausted by the faradic current, but respond again after rest. This electric reaction is quite variable. In some cases it is marked, in others slight. It may be present at one time, and absent at another in the same case. Again, it is often present in a certain group only of the affected muscles. The number of names by which the disease is known is numerous. Among them are bulbar paralysis without anatomical lesions, maladie d'Erb, syndrome d'Erb et Goldflam, myasthenie grave pseudoparalytique (Jolly), chronic progressive bulbar paralysis (Oppenheim). Strümpell[2] called the affection asthenic bulbar paralysis.

The most salient features of the disease are briefly as follows:

ETIOLOGY. Sex has a marked influence. The disease is most frequent in the female. Of the reported cases, there were nearly twice as many females as males. It appears most often between the ages of twenty and thirty years. Only three cases under ten years of age have been reported. One of these was a child of four years (Karplus[3]), and another of five years (Goldflam).[4] A third was a child of eight years (Gowers).[5]

No real cause for myasthenia gravis is known. Some prostrating infectious disease, such as tuberculosis, influenza, typhoid, diphtheria, etc., frequently precedes the affection. Toxic causes, as alcohol, rheumatism, and syphilis, have been assigned, but their significance is unknown. Anæmia, menstrual disorders, and pregnancy were noted in women. Mental strain and anxiety, exertion and migraine, occasionally precede myasthenia gravis.

ONSET. This is usually gradual; but occasionally the symptoms increase quite rapidly, death resulting within a few weeks. Such a case is reported by Devendorf.[6] Weeks, months, or years elapse sometimes before symptoms of the disease appear other than ocular paresis. In Karplus'[7] patient ocular paralysis occurred at intervals for nineteen years before any other signs of the disease were observed.

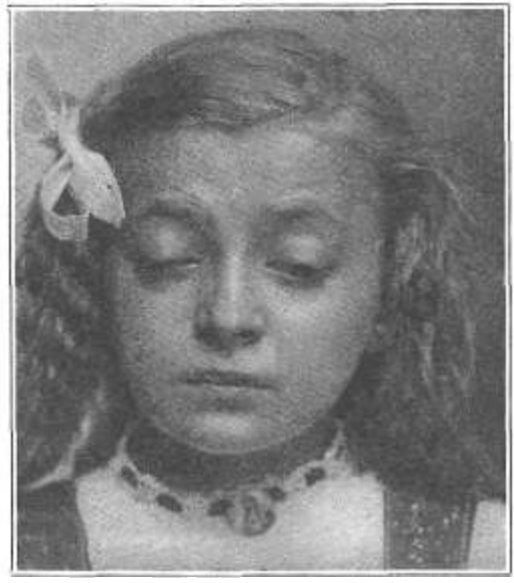
SYMPTOMATOLOGY. An early and most important symptom coming on gradually and insidiously is ptosis. In nearly half the cases this was the first symptom to appear. It was present in over 80 per cent. of all recorded cases. "When it is remembered how easy it is for a patient to overlook a slight ptosis, this proportion

[1] Berl. klin. Woch., 1895, Bd. xxxii.
[2] Deutsch. Zeitschr. f. Nervenheilk, 1896, Bd. viii.
[3] Jahrb. f. Psych. u Neurol., 1897, Bd. xv.
[4] Neurol. Centralbl., 1902, Bd. xxi.
[5] British Medical Journal, 1902, vol. lxxxv.
[6] Deutsch. med. Woch., 1902, Bd. xxviii.
[7] Ibid.

FIG. 1.

Position of the lids when no effort is made to raise them. Note the inability to completely close the lids.

FIG. 2.



Strong effort made to raise the lids. The absence of wrinkles in forehead is very noticeable.

seems all the more remarkable" (Hun).[1] As a rule, the ptosis is unilateral at the onset, but it soon becomes bilateral and more marked on one side than on the other, as in the case reported (Figs. 1 and 2). In the morning after the night's sleep it may not be present, but shortly after the patient rises it rapidly becomes marked, and is always worse toward the end of the day or after looking up for any length of time, when the lids gradually droop. Compensatory action from the occipitofrontalis muscle, present in other forms of ptosis, is wanting, due to its own weakness (Fig. 3). Owing to the ptosis and the weakness of the occipitofrontalis muscle the head is thrown back to enable the patient to see. The

FIG. 3.

Eyes were bandaged for ten seconds. The difference between the two eyes is well marked.

double ptosis and the effort made to see causes a sleepy appearance. Unilateral ptosis is reported by Goldflam,[2] Fajersztajn,[3] Kowjewnikoff,[4] and Raymond.[5] Complete and persistent ophthalmoplegia externa occurs without exception at some period of the disease. Although the ocular paralysis affects the extrinsic muscles of the eye, the intrinsic muscles are never paralyzed. Reaction of the pupils to light and accommodation always seems to be normal. In a doubtful case reported by Brissaud and Lautzenberg[6] the

[1] Albany Medical Annals, January, 1904.
[2] Deutsch. Zeitschr. f. Nervenheilk, 1893, Bd. iv.
[3] Neurol. Centralbl., 1896, Bd. xv.
[4] Deutsch. Zeitschr. f. Nervenheilk., 1897, Bd. ix.
[5] Gaz. des hôpitaux, 1900, tome xxi.
[6] Arch. gén. de méd., Mars, 1897.

light and accommodation reflexes of the pupil were abolished. Inequality of the pupils has been noted, and in a case reported by Buzzard[1] the pupils showed a tendency to oscillatory movements after prolonged convergence. There is frequently an inability to completely and firmly close the lids. This is present in the case herewith reported (Fig. 1). Owing to the weakness of the orbital muscles, diplopia is often present. This is associated rarely with irregular nystagmoid movements, produced by lateral conjugate deviation of the eyes. Strabismus is often present (Fig. 4). A slight prominence of the globe has been observed in a number of

FIG. 4.

Showing the divergence of the right eye.

cases, probably due to the weakness of the recti and the orbicularis palpebrarum muscles. Exophthalmos with symptoms of Basedow's disease was present in cases reported by Jendrassik,[2] Goldflam,[3] Karplus,[4] Oppenheim,[5] and others. The muscles of mastication are very commonly implicated, so that eating is a slow and difficult process from their rapid exhaustion. The muscles of deglutition are often involved, so that food collects in the roof of the mouth and is swallowed with difficulty, and liquids regurgitate through the nose, owing to the weakness of the palate. Choking while

[1] Transactions of the Ophthalmological Society of the United Kingdom, vol. ix.
[2] Arch. f. Psych., 1886, Bd. xvii. [3] Ibid. [4] Ibid.
[5] Monograph, Die Myasthenische Paralyse, Berlin, 1901.

eating is very likely to occur, on account of the diminution in the pharyngeal reflex. Weakness of the pharyngeal muscles is uncommon, but has been observed with the laryngoscope in the cases of Hoppe,[1] Buzzard,[2] and Oppenheim.[3] The speech, at first normal, shortly becomes nasal and the words grow more and more indistinct, until there is complete aphonia. Neither muscular atrophy nor the reaction of degeneration is ever present. Pain is a rare symptom. The muscular symptoms are, as a rule, bilateral. The weakness of the muscles results in their rapid exhaustion upon active movements. Bulbar paralysis is present to a greater or less degree, and finally dyspnœa after exertion is a striking symptom. From this the patients usually die. The phenomenon of muscle tiring and permanent paresis is found in those voluntary muscles which are continually in tonic contraction and have little rest, such as the levator palpebræ, the muscles of expression and mastication. The purely reflex acts of the eye and extremities do not show any abnormal tiring, Jolly,[4] Buzzard,[5] Campbell,[6] and others. This phenomenon of weakness, as a rule, is not present in all of the muscles, but is limited to a few muscles or a group of muscles, as in the case reported. This particular symptom may wholly and unexpectedly remit for several days. Indeed, remissions and exacerbations are the rule, but the weakness is always worse in the evening.

PATHOLOGY. The pathology is vague and uncertain. In the autopsies that have been made there is no evidence that the disease is associated with any lesion of the nervous system. In over half the cases no lesion was demonstrable. Many hypotheses have been brought forward in explanation of the symptoms, but as to the exact nature of the disease we are profoundly ignorant. From the clinical conditions, gross lesions could not be expected.

PROGNOSIS. Judging from the reported cases, the prognosis as regards recovery is practically hopeless. Apparent recovery has been noted, but when we recall the great improvement and apparent recovery lasting weeks, months, or years, and followed by a relapse we must look upon permanent recovery as doubtful. The average duration of the disease is from one to three years. Of the one hundred and twenty cases referred to fifty died.

DIAGNOSIS. The diagnosis is easy in typical cases when the rapid tiring and variation in the intensity of the symptoms with the myasthenic reaction appears; but the diagnosis is especially difficult, and at times impossible, in the early stages of slowly developing and atypical cases. The possibility of hysteria being mistaken for this disease is great, especially when the only symptoms are ptosis

[1] Monograph, Die Myasthenische Paralyse, Berlin, 1901.
[2] Ibid.
[3] Ibid.
[4] Ibid.
[5] Ibid.
[6] British Medical Journal, 1899, vol. i.

and diplopia, appearing and disappearing without apparent cause. Ocular paralyses, rapid tiring of the muscles are rarely found in hysteria, while the myasthenic reaction is not. As in other hysterical paralyses, those of the eyes are characterized by their lack of permanency, their change under psychic influences and their association with sensory disturbances and other hysterical stigmata. In the early stages of the disease it might readily be mistaken for nuclear ophthalmoplegia, and when the ophthalmoplegia alone is present, the diagnosis is extremely difficult. In myasthenia gravis the muscles regain a certain amount of power after rest, but sooner or later the other symptoms of the disease appear. In pseudobulbar paralysis the ocular muscles are not involved, and the myasthenic reaction and rapid tiring are not present.

TREATMENT. The treatment consists first in absolute rest, gentle massage, and measures to maintain a high standard of nutrition. A mild galvanic current has been used, but its benefits are questionable. Many drugs have been tried, but none seems to have any favorable influence over the progress of the disease. The case about to be described illustrates very nicely the ocular phase of the disorder.

The patient, E. M., a female, aged ten years, of American birth, but of Bohemian parentage, was referred to me in November, 1902. At the time of my first examination there was present double ptosis, most marked on the right side (Figs. 1 and 3), paresis of all the extrinsic muscles of both eyes, and a marked divergent squint of the right eye (Fig. 4), with complete preservation of the functions of the intrinsic muscles. The iris reacted to both light and accommodation. The fundi were normal, and save for an error of refraction—O.D. +1.50—3.50 X 180° V. 6/9+: O.S.—1.25 X 180° V. 6/5—the visual faculty was normal. Her history is as follows:

In 1898, when the patient was four years old, she was ill, but nothing further can be learned. Two years following, in 1900, her mother first noticed a drooping of the right eyelid, and a few weeks later the left became affected. She was taken to the Illinois Charitable Eye and Ear Infirmary in November, 1901, and all that the records there show is the following:

" Case No. 108,110, E. M.; mixed astigmatism; ptosis acquired one year; defective motion of all external eye muscles except left external rectus." The child is well nourished, and repeated examinations show nothing abnormal with any other functions of the body. From the beginning there was no evidence of ptosis upon getting up in the morning, but gradually the drooping becomes marked as the patient gets about. Early in the history the ptosis disappeared entirely for a day or two, only to return again. The eyelids can be closed, but not tightly, and, owing to the weakness of the occipitofrontalis, the forehead can be moved but very little. The patient tries to overcome the ptosis by throwing her head back.

With the persistence of the ptosis there was observed a gradual progressive impairment of power in the movements of the eyeballs, but without diplopia. This increased until the eyes became completely fixed in the primary position. At the present time there is about one millimetre of lateral excursion in either eye, but motion is barely perceptible in the vertical. If the eyes are bound lightly with a bandage or even kept closed for a few seconds, the movement of the lids appears normal (Fig. 2), but raising the lids three or four times in succession causes complete exhaustion. The movement of the globes improves only slightly with rest. A feeble myasthenic reaction has been demonstrated at times, and when sought for again was entirely absent. There is no history of tuberculosis, syphilis, or nervous disease in the family. There is nothing abnormal in the motor or sensory distribution of the fifth nerve.

Let us now consider what the nature and seat of a lesion would probably be that would cause an impairment of function of part of the third nerve and also the fourth and sixth on the same side, and do no damage to the structures in the immediate vicinity. An intraorbital lesion of the third nerve, or one involving its intracranial trunk, would not account for it, for the ciliarius or the sphincter iridis would not escape. Could a gross lesion, such as a tumor, meningitis or an area of softening, affect the nuclei of the third, fourth, and sixth nerves, and at the same time not involve the centres for the iris and ciliary muscle, the fifth and seventh or other neutral tracts? To this question we must answer no, excepting that we assume several independent lesions have involved the nuclei of a set of associated nerves on both sides, which is quite improbable. The most rational hypothesis, then, is that the disease is purely a motor one, and that the lesion must be situated either in the muscles themselves or in the motor nuclei. It has been demonstrated by Hensen and others that the innervation of the sphincter of the iris and the ciliary muscles arises from nuclei separate and distinct from those giving origin to the remaining parts of the third nerve. The myasthenic reaction, and the nature and distribution of the symptoms, point to a disturbance in the muscles or the peripheral motor neurons, rather than to a lesion in the motor nuclei. Whether this can be explained as due to the action of a toxin powerful enough to produce symptoms of the disease, and yet produce no demonstrable structural changes, or to lymphoid infiltration of the muscles as found by Weigert,[1] Goldflam,[2] Link,[3] and Hun,[4] is a question unsettled, as yet. Until some definite and characteristic anatomical lesions are proven, we can only theorize.

[1] Neurol. Centralbl., 1901, Bd. xx.
[2] Ibid.
[3] Deutsch. Zeitschr. f. Nervenheilk., 1902, Bd. xxiii.
[4] Ibid.