nostic value is almost nil, because one does not know what it had been like previously. To be of diagnostic value, a series must be taken over a period of from two days to three or four weeks, because the characteristic changes may occur rapidly or slowly, and are some times delayed as long as three or even four weeks. As a general statement, one would be fairly safe in saying in a patient suspected of having coronary occlusion that if the T's remained fixed for three weeks, coronary occlusion could be excluded. In following this rule, one would certainly miss odd cases, but the chances are that most of them would be mild and unimportant. Further, it is necessary to remember that what changes might occur could be caused by other diseases, which therefore have to be excluded. Changes in the take-off, shape, and direction of the T waves due to cardiac infarction may be somewhat closely simulated in any form of active heart disease, including pericarditis; in myxœdema at the commencement of thyroid administration; in an anginal attack, where they last only a few minutes; in digitalis administration; and in any severe illness such as pneumonia, diabetic acidosis, or pulmonary embolism. They have been noted in delirium tremens. They can be produced temporarily in normal people by breathing an atmosphere low in oxygen. The writer has to confess that he has never been able to use the so-called significant Q or S waves for the diagnosis of cardiac infarction. Where they have been seen the diagnosis has already been established by more outstanding changes in the T waves.

When a pain occurs in and is confined to the epigastrium the chance of its being cardiac is greatly increased. In such a case the patient should be put to bed and examined for both coronary and abdominal disease, and the decision arrived at by the preponderance of evidence in favour of one or the other. In case, however, no decision can be reached, or where the case is in an isolated place and facilities for further investigation are wanting, the patient should be confined to bed for four or five weeks, on suspicion of its cardiac origin, especially when there is a very fair probability that it might be cardiac. The mistakes that are made nowadays are the reverse of those made ten or fifteen years ago. Then coronary thrombosis was not diagnosed when it should have been. Now it is diagnosed frequently when it should not be, in cases that obviously have pain due to gall bladder or other abdominal origin. It is a very common tendency when the profession has recently learned a new diagnosis to overwork it.

MYASTHENIA GRAVIS: A CLINICAL REVIEW OF EIGHTY-SEVEN CASES OBSERVED BETWEEN 1915 AND THE EARLY PART OF 1932*

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IN the spring of 1932 Dr. Walter Boothby[1] began his extensive investigation of myasthenia gravis at The Mayo Clinic. Recently, in his eighth report,[2] he published his observations on a series of 82 cases in which the patients had been under his supervision since 1932. As there is no available report regarding the results of treatment in a single large series of cases observed prior to the work of Boothby, it was deemed advisable to review the clinical records of patients examined at the clinic before the use of ephedrine, glycine, and prostigmin. With this plan in mind, the present study was undertaken, in the hope that we might be able to judge of the advance which has been made regarding this disease since 1932.

No attempt has been made in this study to review the literature on myasthenia gravis. Acknowledgment must be made to Miss Harriet Edgeworth[3] who introduced the use of ephedrine in the treatment of this malady. At The Clinic Dr. Henry Woltman was the first to appreciate

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This review includes only those cases of myasthenia gravis which were observed between 1915 and the early part of 1932. They are not to be confused with the cases which have been observed by Boothby since 1932.

the possibilities of ephedrine in the treatment of myasthenia gravis, and he introduced its use in the neurological service. It is a noteworthy fact that for a condition as prevalent and as strikingly characteristic as myasthenia gravis no instances of the disease appear to have been recognized or at least reported in the literature prior to the cases observed by Willis[6] in the seventeenth century, by Wilks,[5] in 1877, and by Erb,[4] in 1879.

The present study includes 108 cases observed between 1915 and 1932. Eighty-seven of these are undoubtedly cases of myasthenia gravis and form the basis of our statistical study. In the remaining 21 the diagnosis was myasthenia gravis. Eleven of the patients in the 21 cases have received ephedrine, glycine, or both, since 1932, and are therefore included in the series of 82 cases recently reported by Boothby. In the remaining 10 there were some unusual features in addition to the myasthenia gravis, so that, with the data available, some doubt might be cast on the accuracy of the diagnosis. These 10 cases are included in the addenda, as they illustrate the more common difficulties encountered in the diagnosis of myasthenia gravis.

ETIOLOGY

An analysis of the cases did not reveal any cause for myasthenia. The records show that in 51 there was no discoverable cause that might be considered as a possible factor in the causation of the disease. In 27 it appeared that some infection, such as a "cold", "flu", tonsillitis, and pneumonia played a precipitating rôle, although the relationship of apparent cause and effect was not always clear. The fact that infection appeared to play a possible rôle in the initiation of symptoms in 31 per cent of the 87 cases is worthy of note, although its exact significance is not clear. It has also been observed that recurring episodes of myasthenia gravis are frequently preceded by some acute infectious process. In 4 cases the first symptoms of muscle fatigue closely followed normal pregnancy. Of the 42 female patients, 25 were married. Seven patients had twelve pregnancies in the course of the disease. In 5 of the pregnancies the symptoms of myasthenia gravis were aggravated; in 4 of the 5 pregnancies the symptoms improved with the termination of the pregnancy or the weaning of the child. During 7 of the 12 pregnancies no changes in the symptoms of myasthenia were noted. At least 4 of the 25 married women were known to have had several uneventful pregnancies prior to the onset of any symptoms of myasthenia. In 5 of the 87 cases isolated precipitating causes were noted, but these were so variable as to be of no seeming importance. Unusual precipitating causes have been recorded in the literature; the occurrence of myasthenic symptoms has been noted following electric shock. The significance of these factors is not known. There was a history of previous syphilitic infection in only one case in the series.

Age, sex, race and heredity.—The ages of the patients at the time of the first onset of the symptoms varied from 10 to 77 years. Of the 87 patients, 7 were in the second, 27 were in the third, 18 were in the fourth, 13 were in the fifth, 12 were in the sixth, 8 were in the seventh, and 2 were in the eighth decade of life respectively. The greatest number were in the third and fourth decades of life. It is usually stated that females are more frequently affected than are males, but in this series, 45 patients were males and 42 were females. It therefore would appear that sex does not play any specific rôle in this disease. So far as we could determine the factor of race had no apparent significance. In no instance in this series of cases was there any evidence of either familial or hereditary factors.

Occupation and geographic distribution.—The occupations of the 87 patients were as follows: 25 were housewives, 17 were farmers, 12 did other manual labour, 12 were executives or did office work, 5 were teachers, 3 were attorneys, 2 were physicians, and 11 followed miscellaneous occupations. There was no close correlation between the occupation of the patient and the situation of the early muscular weakness. Just as frequently as not the ocular signs were likely to be the first symptoms among farmers, while in cases in which the patients followed a more sedentary occupation, weakness of the legs or arms was likely to develop before or in conjunction with ocular disturbances. The distribution of the patients according to residence was in keeping with the general distribution of patients as seen at the clinic. In other words, there was no special environmental or geographic characteristic.

LAPSE OF TIME BETWEEN THE APPEARANCE OF FIRST SYMPTOMS AND THE MAKING OF A CORRECT DIAGNOSIS

The length of time which elapsed between the onset of the first symptoms and the making of the correct diagnosis ranged from one month to 25 years, and varied considerably. For the 87 cases this period averaged four and eight-tenths years. In the majority of cases the diagnosis was made between two and four years after the onset of the disease. Fifteen patients had had the affliction in a mild form for ten years or more before it was correctly diagnosed. The fact that the disease may be present for so many years before the diagnosis is made suggests at once that at least in a fair percentage of the cases the disease process must be relatively mild to escape diagnosis for such a long period of time. It is this remarkable tendency of the disease to have such a variable course as regards severity and duration that makes any deduction regarding the value of treatment a difficult and delicate one. It may well be a surprise to some readers that myasthenia gravis may exist for so many years without more serious consequences, and that it may be present in such a relatively mild form as to go unrecognized for as long as twenty-five years.

RELATIONSHIP OF SYMPTOMS TO OBJECTIVE FINDINGS; EARLY SIGNS

In this series of cases the appearance of the first symptom of myasthenia gravis and the appearance of the first objective sign of the disease paralleled one another rather closely. At times, however, the patient complained of general weakness, or even of weakness referable to a specific group of muscles for some months or even years before any objective evidence of the disease appeared. When the weakness did appear it often did not correspond to the group of muscles to which the subjective symptoms were referred. The relationship of the initial symptoms and the first objective signs of the disease is shown in Table I. In 26 cases the first signs appeared during the first month of the disease. In 29 cases the signs appeared between the first month and the first year; in 16, between the first and second years, in 16, after the second year. Three patients in the last group had noted subjective complaints for 12, 13 and 23 years, respectively, prior to the appearance of objective signs. As we have said previously, it is this tendency for the late development of positive signs which frequently leads to errors in diagnosis. Because of the lack of objective evidence of the disease these patients are frequently considered as "neurotics". It must be confessed that 12 years is a long time to wait for objective evidence of a disease process, but this was necessary in three cases in this series.

TABLE I.
INITIAL SYMPTOMS AND SIGNS IN EIGHTY-SEVEN CASES OF MYASTHENIA GRAVIS

Initial symptoms	
Symptoms referable to ocular disturbances	36
Symptoms referable to weakness of the limbs	24
General weakness	11
Bulbar weakness	9
Facial weakness or weakness of the jaws	5
Miscellaneous symptoms	2
Total	87
First objective signs	
Ocular weakness	58
Pharyngeal or bulbar signs	13
Weakness of the limbs	11
Weakness of the jaw	5
Total	87

In slightly more than a third of the cases the first symptom was referable to the ocular muscles, while in two-thirds of the cases the first objective signs were related to these muscles. Weakness of the masseter muscles, which is said to be very characteristic of myasthenia gravis, was an early sign in only 14 per cent of the cases.

MUSCLES MOST COMMONLY AFFECTED; OPHTHALMOPLEGIC TYPE OF MYASTHENIA GRAVIS

The groups of muscles involved in this series of cases and the percentage of cases in which they were involved are as follows: ocular muscles 78 per cent, facial muscles and masseter muscles 61 per cent, muscles of deglutition and phonation 58 per cent, muscles of the arms 29 per cent, muscles of the legs 24 per cent, and muscles of the neck and shoulders 17 per cent. The groups of muscles involved were determined during the various visits which the patients made to the clinic. It has been noted that in a given case, if there are periods of improvement and recurrence of weakness, the muscular weakness has a tendency to maintain a fairly constant pattern and the recurring episodes affect the

same muscles, although the severity of the weakness may vary considerably in successive spells of weakness. No ocular findings of any type were noted in 7 cases. In 8 cases the reverse was true, that is, the only objective evidence of myasthenia gravis was the presence of ocular phenomena. It has been observed that in several cases in which ocular disturbances were the only objective signs of myasthenia gravis involvement of other muscles has not been noted. In such cases in which the disease is of the external ophthalmoplegic type it may be mistaken for various other conditions in which ophthalmoplegia is an outstanding symptom.

REFLEX DISTURBANCES

No unusual reflex disturbances were observed in any of the cases. The deep tendon reflexes were occasionally decreased or even increased, but never absent. In a few cases the abdominal reflexes could not be obtained.

CHANGES IN THE CEREBROSPINAL FLUID

In the 32 cases in which the spinal fluid was examined, the study included the Kolmer and Kahn tests, the Nonne-Apelt reaction, a cell count, an estimation of the amount for the total protein, a colloidal gold test, and estimations of the pressure. In 28 of the cases the spinal fluid was entirely normal. In 3 there was a slight increase in the number of cells, that is, there were 6, 8, and 11 cells per cubic millimetre of spinal fluid, respectively. In one case the value of the total protein was 100 mg. per 100 c.c. of spinal fluid. It therefore is evident that the spinal fluid is invariably normal in cases of myasthenia gravis.

ELECTRIC REACTIONS

Much has been written regarding the value of the electric reactions in cases of myasthenia gravis. Unfortunately, electric examination was not carried out regularly in these cases, and our figures, therefore, are not conclusive. The failure to test the electric reactions in these cases seems to have been attributable to the assumption that the electric reactions were not necessary to make a diagnosis in a case in which the clinical findings were typical, and that they would not aid in making the diagnosis in a case in which the diagnosis was doubtful. The electric reactions were tested in 24 cases. In 11 cases the typical reaction of myasthenic muscle fatigue was present; in 4 cases the reactions were recorded as doubtful, and in 9 cases there was no myasthenic reaction. In several of the cases in which no myasthenic reaction to the faradic current could be obtained only the ocular and facial muscles showed evidence of the disease process. It may be that the application of the electric tests to the muscles of the limbs in these cases was not a fair procedure, and that the tests should have been applied to the affected muscles.

ROUTINE MEDICAL EXAMINATION AND LABORATORY TESTS

The usual routine examinations, including medical tests and laboratory investigations, were carried out in these cases. From these studies very little helpful information was derived, unless it was the fact that such examinations as a rule failed to reveal any abnormality. The average range in the value for the systolic blood pressure was between 105 and 130 mm. of mercury. In a few instances the value for the systolic pressure was as high as 180 mm., but this occurred only among elderly patients. Examination of the blood, including the flocculation test for syphilis, estimation of the concentration of hæmoglobin, and erythrocyte and leukocyte counts, did not disclose anything of significance. Routine roentgenological examination of the thorax did not reveal any abnormality. In no instance was the shadow of a tumour of the thymus gland observed. In several cases a substernal thyroid shadow was noted. The basal metabolic rates varied from −20 to +20. Analysis of the gastric contents revealed that the value for total acidity was 80 and for free hydrochloric acid was 30 (Töpfer). Routine examinations did not reveal any evidence that would aid one in determining the cause or nature of this disease process. There is a suggestion in the history of these patients that infections may play a possible rôle in the etiology, but the clinical examination did not furnish any corroborative evidence.

Biopsy.—Biopsy was performed in 5 cases. In 4 the microscopic examination of a section of the affected muscle did not reveal anything of importance; in the remaining case the biopsy disclosed an accumulation of lymphocytes or so-called lymphorrhages. It was suggested that

these might be nuclei of degenerated muscle. The presence of an increased number of lymphocytes in the affected muscles has been frequently referred to, but it is not a constant finding and its significance is not known.

PSYCHIC REACTIONS

The psychic reactions are not characteristic in cases of myasthenia gravis. As one might well anticipate, these patients, because of their physical incapacity, have a tendency to emotional disturbances, either of an anxiety or depressive type. These reactions are understandable when one realizes the seriousness of the affliction. The psychic reactions may manifest themselves in varying degrees, but as a rule they may be considered within the range of normal mental reactions. Seven of the patients in this series were sufficiently depressed to warrant some special comment by the physician. One of them committed suicide.

DIAGNOSIS

The diagnosis of well-established myasthenia gravis is relatively easy. In many cases the condition is not typical, and especially during the early months or even years of the disease the diagnosis may present considerable difficulty. The most frequent incorrect diagnosis during the early stages of the disease probably is "psychoneurosis". The diagnoses which had been made before the patients came to the clinic are of interest. In 41 cases no accurate diagnosis had been made, but in some of these the disturbance had been considered functional. A positive diagnosis of myasthenia gravis had been made in 11 cases, and in 9 a tentative diagnosis of myasthenia gravis had been made. Thus, in 20 of the cases the disease had been correctly diagnosed before the patients came to the clinic. In 7 cases the patients had been treated for functional disorders, but, as stated previously, the condition had been considered functional in several other cases in which no accurate diagnosis had been made. In the remaining 19 the diagnoses had been as follows: ocular palsy in 5, progressive muscular dystrophy in 3, bulbar palsy in 3, multiple sclerosis in 2, goitre in 2, and tumour of the brain, facial diplegia, apoplexy, and arteriosclerosis of the central nervous system in one case each. This list of diagnoses illustrates the usual difficulties encountered in the differential diagnosis of myasthenia gravis.

In 7 of the cases the "admission diagnosis" was as follows: psychoneurosis in 2, bulbar palsy in 2, progressive muscular dystrophy in 1, ophthalmoplegia resulting from a focal lesion in 1 case, and arteriosclerosis of the central nervous system in 1. In two other cases a diagnosis was not made when the patient was first admitted.

It is well to bear in mind that an early diagnosis of myasthenia gravis may be very difficult to make, as the symptoms may be essentially of a subjective character and the examination may reveal little that is objective. It is also important to remember that in a small group of cases the symptoms are very mild and chronic and that they may be present for years before their significance is appreciated. It is certainly true that not infrequently myasthenia gravis may present itself under the guise of marked general fatigue, and to the chagrin of the physician his diagnosis of neurasthenia, chronic nervous exhaustion, and so forth, returns to haunt him in the form of an organic disease. Conversely, it must be emphasized that every chronic fatigue state is not a form of myasthenia gravis, and although the patient may improve as a result of what may be considered proper treatment for myasthenia gravis the diagnosis of the disease is not established on therapeutic grounds.

REMISSIONS

It is a common statement that one of the characteristic features of myasthenia gravis is the occurrence of a partial or complete remission of the myasthenic symptoms, which may vary in duration from months to years. In this paper the term "complete remission" has been applied to seemingly complete recovery which has lasted for more than a month and has permitted the patients to resume their former occupations. The term "partial remission" has been used to indicate some improvement which has lasted for months or years. Moderate fluctuations of symptoms have not been classified as partial remissions. These fluctuations have been considered normal variations of the disease process. The figures regarding remissions are based to a great extent on the information obtained from the patients after they were dismissed from the clinic. The figures, therefore, are not entirely accurate, but they should serve as a basis of comparison for future work.

In 44 of the cases no mention was made of a remission, and in 3 other cases the patients failed to reply to the questionnaires. Twenty-seven patients had 43 complete remissions, which ranged from more than one month to 15 years in duration. The average duration of a complete remission was two and two-tenths years; the majority of them lasted less than one year. It is of special interest that in 5 of these cases the remissions lasted 4, 7, and 15 years respectively. These figures appear to be rather high and it may be that some of these complete remissions should be classified as partial remissions. Thirteen patients had 17 partial remissions which lasted from less than one month to 16 years, the average duration being one and five-tenths years. The majority of these remissions lasted less than six months. Needless to say, it is this tendency to remissions in this disease that makes the benefits of any form of treatment so difficult to evaluate. The remissions which have been noted in this series of cases might be termed "spontaneous" remissions.

COMPLICATIONS

No unusual complications were noted in this series of cases of myasthenia gravis. It was observed, however, that any accompanying illness exaggerated the existing symptoms and also tended to precipitate added myasthenic symptoms.

THE RESULTS OF TREATMENT

It was possible to trace all but three of the patients in this series of cases. Of the 84 patients who could be traced, 34 are known to have died; 18 of these were females and 16 were males. The ages of these patients at the time of their death ranged from 13 to 72 years. At the time of their death, 1 of the patients was in the second decade, 7 were in the third decade, 10 in the fourth, 7 in the fifth, 4 in the sixth, 4 in the seventh, and one was in the eighth decade of life, respectively. The majority of deaths occurred in the decades of life in which the disease is most frequently encountered. The duration of the illness up to the time of death varied from six months to twenty-two years; the average duration was four years and six months. The cause of death in the 34 cases was recorded as follows: the disease itself in 24 cases; cause unknown in 3 cases; cardiac failure, suicide, respiratory failure, undulant fever, nephritis, bulbar palsy, and strangulation in 1 case each. Of the remaining 50 patients who could be traced 12 reported that they were alive, but they did not furnish sufficient information to permit us to appraise the exact status of their physical condition. Thirteen reported that their physical condition was the same as it had been at the time of their last visit to the clinic, and 10 reported that they were improved or had had a remission of symptoms. Eight patients reported that their condition was worse than it had been, and 7 reported that the course of the disease had fluctuated since they had last visited the clinic.

The 34 deaths in this series of cases, which was observed between 1915 and the early part of 1932, and the present physical condition of the remaining 43 patients should be contrasted with the results obtained by Boothby since the early part of 1932. In his eighth report on myasthenia gravis, Boothby reported the following results: of the 82 patients who had myasthenia gravis and who had been under his observation four years since the early part of 1932, 41, or 50 per cent, were employed at full-time or part-time work, 15 were able to be up and about their homes, 2 were confined to their rooms, 7 had been lost track of, and 17 had died. Of the 17 who died 5 should be excluded from consideration of the effect of treatment because 1 died immediately after he came to the clinic before therapy could be started, and 4 abandoned treatment or died of other causes not directly attributable to the myasthenic syndrome.

FINDINGS AT NECROPSY

Necropsy was performed in 3 cases. The reason for so few post-mortem examinations is because the great majority of the patients died at home and no necropsy was performed. The post-mortem findings in the 3 cases were uniformly negative. In one case it was noted that the muscles contained more fat than usual and that occasional lymphocytes were present in the muscle bundles. In one of these cases the myasthenia gravis was of a severe type; the entire duration of the disease was only nine weeks. Hyperplasia of the thymus gland is not an unusual finding and post-mortem examination has revealed the presence of a "thymic

tumour'' in a small group of cases, but in the 3 cases in this series in which necropsy was performed no disturbance in the ductless glands was noted.

TREATMENT

The treatment of myasthenia gravis until very recently has been a source of discouragement to the patient and a cause of nightmare for the physician. The physician has felt helpless, but in his desire to aid the patient he has resorted to the use of various drugs and remedies, all of which have seemed powerless to stem the course of the illness. Strychnine and thyroid extract probably are the drugs most frequently used. Diets, baths, electricity, and massage have had their advocates. Operations on the thyroid gland have been recommended, as has the application of roentgen therapy to the region of the thyroid and thymus glands. Recently, serums and vaccines have been employed in an endeavour to combat some hidden infection. All foci of infection have been removed, but the results of treatment have remained the same. The same may be said of organotherapy, as the recent administration of extracts of the suprarenal gland, tissue extracts, and various other products. In 1930, Harriet Edgeworth announced the results in her own case following the administration of ephedrine sulphate. Since then Boothby and others have reported their results with ephedrine and glycine. Benzedrine sulphate, prostigmin, and vaccines recently have added to our therapeutic armamentarium. The results of treatment since 1930 have been so striking and the renewed interest in this disease has been so enthusiastic that it would seem that we might be on the threshold of a definite understanding of this disease and a means of intelligently combating it.

ADDENDA

In addition to the 87 cases of myasthenia gravis which form the basis of this study we have reviewed 21 other cases in which a diagnosis of myasthenia gravis was made. These 21 cases have not been included in the group of cases for analysis, because of various complicating factors. Eleven of the 21 patients were first examined prior to 1932, but as they subsequently received ephedrine, glycine or both, they are included in the series of 82 reported by Boothby. In two cases there was an associated muscular dystrophy. This complication has been observed previously and is not to be confused with the Landouzy-Déjérine type of muscular dystrophia that may simulate myasthenia gravis. In the remaining 8 cases another condition was considered in the diagnosis, and these cases therefore have not been included in the analysis, as the diagnosis of myasthenia gravis was not positive and the information which was obtained after the patients left the clinic was not accurate enough to aid us in making a definite diagnosis. The conditions which were considered in the differential diagnosis in these cases were polioencephalitis, ''acute myasthenia gravis'', external ophthalmoplegia, anorexia nervosa, psychoneurosis, exophthalmic goitre, simple depression, and multiple sclerosis. As has been stated previously, these represent the more common conditions which must be considered in the differential diagnosis of myasthenia gravis.

SUMMARY

An analysis of these cases has not furnished any helpful information regarding the possible etiology of myasthenia gravis. It was observed that some form of infection did appear to act as a precipitating factor in 31 per cent of the cases. The age of the patient at the time of the onset of symptoms varied from 10 years to 77 years; in the majority of cases the patients were affected during the third and fourth decades of life. Myasthenia gravis may represent an acute process which has an early fatal termination, or it may run a long mild course. The average lapse of time between the first appearance of symptoms and the making of a correct diagnosis was four and eight-tenths years. Fifteen patients had symptoms of the disease for ten years before the condition was correctly diagnosed. This tendency for the disease to be insidious in onset and very mild during the first few years frequently results in an early incorrect diagnosis; the condition often is considered functional in its early stages. In cases in which the disease is of the ophthalmoplegic type, it is especially prone to be chronic and relatively mild. The most frequent early sign of the disease is a disturbance in the ocular muscles. Weakness of the masseter muscles was present as an early sign in only 14 per cent of the cases. Twenty-seven patients had remissions; the average duration of the remissions

was two and two-tenths years. In three instances the remission lasted for 5, 7, and 15 years respectively. In 20 of our 87 cases a correct diagnosis had been made before the patients came to the clinic; in 7 the diagnosis which was made when the patients were first examined at the clinic had to be changed subsequently; and in 2 others no diagnosis was made when the patients were first examined. In the differential diagnosis of myasthenia gravis functional disorders are the most common source of error. The association of muscle dystrophy with myasthenia gravis has been observed; this should not be confused with primary dystrophy.

Thirty-four deaths occurred in the 87 cases of myasthenia gravis observed between 1915 and the early part of 1932. In these 34 cases the duration of the disease varied from 6 months to 22 years, the average duration being four and a half years. As neither any therapeutic measure of value nor any practical or consistent regimen for treating patients who had myasthenia was available at the time this series of cases was observed this mortality represents essentially that of the untreated disease. The results here recorded should be compared with the results obtained by Boothby in a subsequent series of 82 cases of myasthenia gravis in which the patients were treated subsequent to 1932 by a systematic regimen embodying the use of the new therapeutic agents now employed in the treatment of myasthenia gravis.

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A PRELIMINARY REPORT ON GLANDULAR THERAPY IN GYNÆCOLOGICAL CONDITIONS*

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THIS paper is a report of work which has been done in the Gynæcological Clinic of the Women's College Hospital in 1936. I have used the word "preliminary" with special intent as there are phases of endocrine therapy which will take a much longer period to demonstrate their value. However, certain results have been obtained which have definite therapeutic value and therefore should be discussed now. As this is entirely a clinical report I have omitted the history of work already done in this field and have only touched briefly on the action of the hormones used.

Let me remind you briefly of the action of the hormones concerned with menstruation. The anterior pituitary hormone, which has two stimulating factors known as prolan A and prolan B. A is the follicle-stimulating factor which acts on the ovary to produce the follicular hormone "œstrin". B is the luteinizing factor which in the same way stimulates the ovary to produce the corpus luteum hormone "progestin". Œstrin acts directly on the endometrium of the uterus, causing the proliferative phase. Progestin carries on the stimulation of the endometrium of the uterus to the pregravid or secretory phase. Ideally, œstrin activity stops and progestin activity begins when the Graafian follicle ruptures. Dr. Kurzroh has a good diagram in the June number of the *American Journal of Obstetrics*, 1935.

In our work we used three preparations (1) *theelin in oil*—2,000 units per c.c. Theelin is a chemically pure crystalline œstrogenic hormone, ketohydroxyestrin, isolated from pregnancy urine—(a unit being the amount of hormone necessary to produce œstrus with cornification, as judged by vaginal smears in an ovariectomized sexually mature rat). (2) *Antuitrin S.*—This is the anterior pituitary-like gonad-stimulating hormone. It is derived from pregnancy urine and is not identical with the gonadotropic principle of the anterior pituitary itself, but is very closely related to it. (3) *Antuitrin gonado-*

* A paper read before the Section of Obstetrics and Gynæcology, Toronto Academy of Medicine.