

# Myasthenia Gravis

## MYASTHENIA GRAVIS: ITS TREATMENT BY A COMBINATION OF PROSTIGMIN AND GLYCINE-EPHEDRINE THERAPY.

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WITHIN recent years, interest has been aroused in the treatment of myasthenia gravis. This has been chiefly due to the results reported by Walker<sup>1</sup> in this country and Boothby<sup>2</sup> in America.

Walker found that the injection of physostigmine produced an immediate increase of muscular power in patients with myasthenia, but that the effect was transient, so that in a few hours the asthenia reappeared as marked as ever, and lasted until the injection of physostigmine was repeated. Prostigmin, an analogue of physostigmine, was preferred as it can be given in much larger effective doses with less toxic effects. Later observations by Laurent and Walker<sup>3</sup> have shown that the oral administration of large doses of prostigmin was also successful in increasing muscular strength. The disadvantage of prostigmin is its liability to produce abdominal pain, but this Laurent and Walker have been able to avert, either by giving atropine with the large doses, or by using smaller doses of prostigmin more frequently.

Boothby, on the other hand, has obtained very encouraging results by the use of glycine and ephedrine.

The following two cases are reported because the result of giving prostigmin and glycine in succession has been in them so successful that it appears that this may be the method of choice in most cases, and also the fact that the maintenance dose of glycine can be gradually reduced.

### CASE I.

A married woman, aged 50 years, was admitted to Glasgow Royal Infirmary on 8th April, 1935. Her illness began at the end of 1933 with difficulty in swallowing and a feeling of fatigue, especially towards evening. During the following year she gradually developed difficulty in chewing and talking.

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After reading for a few moments the letters became blurred, but there was no diplopia. The lower jaw drooped. From September, 1934, she gradually became weaker until, on admission, she was completely bed-ridden.

*Examination.*—The patient was completely helpless, being quite unable to do anything for herself. She had an immobile facial expression with bilateral ptosis. The lower jaw drooped, and she could make no attempt to whistle. The voice was thick and she had difficulty in articulating her words. The eyelids could not be closed tightly and could be separated easily. She was unable to hold her head up, or sit up. Feeding required two nurses, one to hold her up, and the other to feed her. The Wassermann reaction was negative.

*Summary of Treatment.* On 12th April, 1935, she was given 2 c.c. of prostigmin hypodermically, and the result was dramatic. Within three minutes she was able to sit up in bed without assistance. Speech became more distinct. Within ten minutes she able to eat a meal, including a chop, the first solid food she had had for a year. The ptosis disappeared, and she was able to whistle. By the end of 3 $\frac{3}{4}$  hours the effect had passed off, and she was in an even weaker state than before.

The dynamometer readings were as follows:—

				Right Hand	Left Hand
Before the injection of 2 c.c. prostigmin				0	0
3 minutes after	do.	do.		0	0
5 do.	do.	do.		5	2
15 do.	do.	do.		34	32
60 do.	do.	do.		20	20
90 do.	do.	do.		20	20
120 do.	do.	do.		18	18
180 do.	do.	do.		0	0

Evacuation of the bowels occurred from 20 to 30 minutes after each injection, but there was no abdominal pain noted. The daily dose of prostigmin was continued, and she was dismissed home on 2nd May, 1935, to carry on the treatment under her own doctor, Dr. W. T. G. Davidson, of Shettleston. For three months she was given 2 c.c. prostigmin hypodermically daily, and during this time she was only able to leave her bed during the four hours after the injection. At the end of three months her doctor gave her by mouth 7 $\frac{1}{2}$  grms. glycine plus  $\frac{1}{2}$

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gr. ephedrine, in addition to the 2 c.c. prostigmin, the latter being given just before the mid-day meal and the former at 6 p.m. After two weeks of this treatment, the prostigmin was stopped, and the glycine and ephedrine only were given. The effect of glycine was noted to be more gradual in its onset, more sustained, and in her own words "more natural." After prostigmin she felt her movements more mechanical, "like a Robot." For the next nine months she continued to receive  $7\frac{1}{2}$  grms. glycine and  $\frac{1}{2}$  gr. ephedrine daily, and at the end of this time she felt so much improved that it was decided to give them every other day. She continued to improve on this until to-day she is able to live an ordinary life, doing shopping, housework, &c.

The interesting features in the treatment of this patient may be summarized as follows:—She responded rapidly to the injections of prostigmin, but in the intervals between the injections, the myasthenia returned in full force. The transfer to glycine and ephedrine was accomplished without any relapse, and indeed was characterized by the absence of the spells of muscular weakness which accompanied the prostigmin therapy. Since the institution of glycine and ephedrine she has improved to the extent of that she is able to do shopping and carrying parcels. A noteworthy fact is that the administration of glycine and ephedrine has been reduced till now she is taking a dose every other day, and maintaining what is apparently perfect health.

### CASE II.

A single woman, a typist, aged 22 years, was admitted to Glasgow Royal Infirmary on 18th January, 1936, complaining of muscular weakness, difficulty in swallowing, and drooping of eyelids of three months' duration.

Three months before admission patient noticed a drooping of her right eyelid, especially towards evening. A month later she experienced difficulty in swallowing and weakness of her arms, her speech became thick, and there was occasionally diplopia.

On admission she lay comfortably in bed. There was slight right-sided ptosis. Face was immobile and expressionless. Weakness of the arms became more marked on repeated movement.

The Wassermann reaction was negative.

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*Summary of Treatment.*—One cubic centimetre of prostigmin was injected twice daily for five days. After each injection there was considerable improvement in general well-being. The ptosis disappeared, she was able to chew, and the voice lost its nasal quality. The improvement lasted about four hours. At the end of five days the prostigmin was stopped and she was given  $7\frac{1}{2}$  grms. glycine and  $\frac{1}{2}$  gr. ephedrine twice daily. The improvement on this was much more sustained, and at the end of five weeks she was dismissed home well. After being at home a month the dose was reduced to once daily and this she found was sufficient.

This patient was suffering from a much milder degree of myasthenia. She showed similar features to that of Case I. She was given prostigmin with good effect for five days, and thereafter the treatment was changed to glycine and ephedrine, and this latter form of therapy was so successful that she is now able, after fourteen months, to carry on a normal life.

The experience with these two patients confirms Boothby's views as to the efficacy of glycine and ephedrine therapy in myasthenia gravis. In view of the fact that these substances are non-toxic, they are preferable to prostigmin.

Prostigmin, however, has a much more rapid action than glycine and ephedrine, and it therefore appears more profitable to commence the treatment of myasthenia with prostigmin so that the patient is better able to take and utilize his food, and is thus brought into a state of better nutrition. Thereafter, glycine and ephedrine therapy, with its more persistent effect, is capable of maintaining and even improving muscular power. Once the full effect of glycine is obtained, a gradual and cautious reduction in dosage is possible without deterioration.

### SUMMARY.

The case-histories of two patients with myasthenia gravis are reported. Successful results were obtained at first with prostigmin and then with glycine and ephedrine. In both patients the dosage of glycine was later reduced.

It is tentatively suggested that a course of prostigmin may be of advantage before commencing glycine and ephedrine.

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I have to thank Dr. J. C. Middleton for permission to publish these cases, and Dr. W. T. G. Davidson for permission to follow up Case I.

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## REFERENCES.

- <sup>1</sup> Walker, M. B., *Lancet*, 1934, *i*, 1,200.
- <sup>2</sup> Boothby, W. M., *Arch. Int. Med.*, 1934, *liii*, 39.
- <sup>3</sup> Laurent, L. P. E., and Walker, M. B., *Lancet*, 1936, *i*, 1,457.