

[Walker MB \(1934\)](#). Treatment of myasthenia gravis with physostigmine. *Lancet* 1:1200-1201.

Key passages

TREATMENT OF MYASTHENIA GRAVIS WITH PHYSOSTIGMINE

To the Editor of THE LANCET

SIR,—The abnormal fatiguability in myasthenia gravis has been thought to be due to curare-like poisoning of the motor nerve-endings or of the "myoneural junctions" in the affected muscles. It occurred to me recently that it would be worth while to try the effect of physostigmine, a partial antagonist to curare, on a case of myasthenia gravis at present in St. Alfege's Hospital, in the hope that it would counteract the effect of the unknown substance which might be exerting a curare-like effect on the myoneural junctions. I found that hypodermic injections of physostigmine salicylate did have a striking though temporary effect.

Mrs. M., aged 56, had had a previous attack of myasthenia gravis, lasting about six months, 14 years ago. Gastric ulcer four years ago. Non-specific infective arthritis seven months ago, now improved.

Towards the end of last February she found that she was unable to hold her shopping bag, and that her head used to fall forwards when she knelt to do the hearth. She had to remain in bed after March 18th, and had difficulty in sitting up. Her jaw then began to droop, she had to hold it up with her hand, and the left eyelid began to droop. Speech became indistinct when she was excited, swallowing was difficult, and fluid sometimes regurgitated through her nose. She was admitted to the hospital on March 28th, and a few days later weakness came on in the middle and ring fingers of both hands. The weakness is much increased by excitement, and is lessened by rest. It becomes worse as the day goes on. There is no wasting, and the tendon reflexes are all present. The masseters respond slightly or not at all to faradism; a myasthenic reaction has been obtained in the left deltoid. Radiograms show obsolete pulmonary tuberculosis. The thymus is not enlarged.

On April 11th treatment with hypodermic injections of physostigmine salicylate, gr. 1/60 once a day, was begun. In from half an hour to an hour after the injection the left eyelid "goes up" (see Figure), arm movements are much stronger, the jaw drops rather less, swallowing is improved, and the patient feels "less heavy." The effect wears off gradually in from 2-4 hours. With injections

of gr. 1/50 the improvement is greater, and it lasts for 4-5 hours. Still greater improvement, lasting for 6-7 hours, followed an injection of gr. 1/45, but the patient felt rather faint and trembly, her "inside seemed all on the work," and she felt as if "something were going to happen." These feelings did not completely disappear till an hour after the injection. In all, 26 injections of physostigmine salicylate have been given. The effect is not quite uniform; on two occasions injections of gr. 1/45 and gr. 1/60 failed



Before injection the patient cannot raise her left eyelid. Thirty minutes after it the eye is fully open. (The photographs are reproduced from a cinematograph film and are reversed left for right.)

to produce any obvious effect. She feels better and more cheerful since the injections were begun.

Given by the mouth, physostigmine salicylate gr. 1/60 produced no obvious effect, but an hour after gr. 1/30 slight improvement occurred. No improvement followed control injections of water, pilocarpine gr. 1/20, strychnine gr. 1/30, adrenaline $\frac{1}{5}$, ephedrine gr. $\frac{1}{2}$, or acetylcholine 0.05 and 0.1 g.

I think that this effect of physostigmine on myasthenia gravis is important, though it is only temporary, for it improves swallowing and might tide a patient over a respiratory crisis. It supports the opinion that the fatiguability is due to a poisoning of the motor end-organs, or "myoneural junctions,"

rather than to an affection of the muscle itself. It may be significant that physostigmine inhibits the action of the esterase which destroys acetylcholine. I have not had the opportunity of treating another case to confirm the findings. The administration of other drugs whose action resembles that of physostigmine is under consideration. It is also possible that physostigmine might be of some service in botulism and in cobra poisoning, in both of which a curare-like poisoning of the "myoneural junctions" of the respiratory muscles has been stated to be the main cause of death.

I wish to thank Dr. Philip Hamill for his interest and advice, and Dr. W. D. Wiggins, medical superintendent of the hospital, for permission to publish the case.

I am, Sir, yours faithfully,

M. B. WALKER.

St. Alfege's Hospital, Greenwich, May 12th.