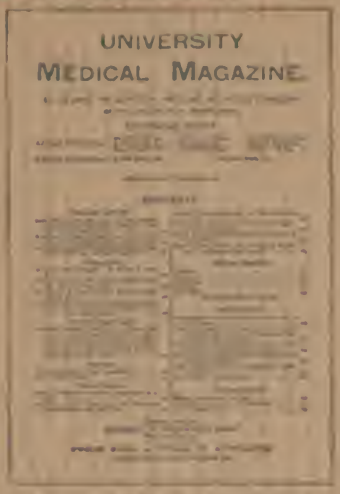

THE TREATMENT OF CHOREA BY LARGE DOSES OF QUININE.

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THE TREATMENT OF CHOREA BY LARGE DOSES OF QUININE.[1]

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Of the various theories that have been advanced from time to time in the effort to elucidate the etiology of chorea and to localize the affection, that is, to ascribe to the choreic movements either a cerebral, or a spinal, or a conjoined origin, that of a diminution or loss of spinal inhibition recently proposed by Professor H. C. Wood in a contribution read before the Philadelphia Neurological Society, and published in the *Journal of Nervous and Mental Diseases* for the month of April, may be accepted as pre eminently a rational one: a theory that is based upon sound scientific investigation and deliberate ratiocination. We would invite a perusal of this very interesting paper, as giving in a more concise and intelligent manner than any resumé we could offer the various steps that led up to the enunciation of the theory suggested. In the meanwhile permit us to review briefly some of the principles involved in this line of study of the motor function of the cord, with its physiological and pathological manifestations.

It appears to be a fundamental law that certain highly specialized cells of the nervous organism have relegated to them powers that are dominant, whose function it is to dominate and regulate other cell-groups not so highly specialized in the assignment of the complex workings of the body. Especially is this law exemplified in the familiar manifestations of the well known cardio-inhibitory centre of the vagal nucleus, and in the intensely interesting and intricate phenomena of thermotaxis. That group of cells to which has been allotted the power of inhibiting the motor function of the spinal cord is designated as Setschenow's centre, which, in the frog, is placed in the optic lobes, and in man and the higher vertebrates is believed to be situated somewhere in the corpora quadrigemina or medulla oblongata. Whatever may be its precise location, it is undoubtedly true that stimulation of this portion of the brain substance will be followed by a marked diminution in the reflex activity of the cord, thus demonstrat-

[1] Read before the Section of Diseases of Children of the American Medical Association, at Milwaukee, June 7.

ing at once the dominating influence of the centre over the motor tracts of the cord beneath.

Spitzka, in the "Reference Handbook of the Medical Sciences," has aptly said: "The spinal cord is essentially a segmental organ;" in the typical vertebrate it may be regarded as made up of a series of nerve centres, fused into a column, "each centre corresponding to a somatic segment, with which it is connected symmetrically by a pair of spinal nerves. Each one of these spinal segments corresponds in its topographical situation with the somatic segment which its nerves supply, and these nerves take a direct transverse course, leaving the cord at right angles to traverse the intervertebral foramina, and thus reach their somatic destination."

Stimulation confined to any one of these spinal centres—thus directly or absolutely augmenting its motor power, or its function of motor discharge—or the cutting off from any one such centre of the inhibitory action of the dominant centre in the brain above—thus primarily, indirectly or relatively, and secondarily, absolutely increasing its motor power—will be accompanied by spasmodic muscular contraction in the somatic segment supplied by the implicated centre. This is self-evident. Now, generalizing, suppose that the direct stimulation be applied to the spinal centres as a whole, the entire cord, simultaneously, or that the inhibitory action instead of being removed from a single spinal centre be very perceptibly diminished, or absolutely cut off from the entire cord, and it will go without saying that all of the somatic segments supplied by the spinal motor nerves will be involved in the exaggerated discharges of motor force, and that the muscular system of the body will, so to speak, run riot.

Professor Wood, from his studies in this direction, would ascribe to chorea some such origin as this: He suggests that the direct cause of the affection lies in a disturbance or overbalancing of the equilibrium that normally exists between the motor power of the spinal cells and the inhibitory apparatus of the spinal cord located in the so-called Setschenow's centre of the brain, the latter in choreics being involved in a paresis more or less marked. During inhibition the function of an organ is restrained; during paralysis it is abolished. The amount of disturbance will depend entirely upon the degree of loss of inhibition. Thus may be accounted for the varying grades of choreic manifestations, from the slightest case of so-called spinal irritation, with the characteristic unrest and ebullition of nerve force, and the exaggerated reflexes of the neurotic individual, to the grave cases of chorea major, with absolute loss of control of voluntary muscular effort, and finally, diminished or absent reflexes from exhaustion and depression of the entire motor area of the cord.

Nowhere is the perplexing uncertainty that surrounds the true etiology of chorea better demonstrated than in the very recent work of Landon Carter Gray. In it he gives a varied list of causes of the disease, covering the most remote possibilities, and including such unsatisfactory etiological factors as the seasons, the emotions, malaria, race, eye strain, as well as the more definite causes, trauma, articular rheumatism, imitation and heredity. After such an array we would naturally expect to hear him say that "although certain cerebral changes have been well described in the chronic and fatal cases, as well as of the disease in animals, there has never been any approach to a description of the pathological alterations that would explain the movements of the ordinary cases of chorea of the Sydenham and athetoid types." We would suggest that at least an intimation to this "approach" is made by such an explanation as the ingenious inhibitory theory of Professor Wood.

So much, however, for the physiology and pathology of the subject; now for the direct application of the principles thus hinted at, for, as far as is possible, all therapeusis should be based upon the results of physiological investigation and its ultimate rational conclusions. Accepting the premise, and regarding chorea as due in all probability to a diminution or loss of the inhibitory power of Setschenow's centre, it is evident that our efforts, therapeutically, should be directed toward the employment of such remedies as will tend to increase or restore the diminished or lost inhibitory power. Hitherto the drugs that have been exhibited in the treatment of chorea have been of two classes: either those whose action upon the nervous system has been confined to the motor nerves—direct paralyzants of the motor nerves and their peripheral filaments; or those whose physiological effect upon the nervous organism has been that of a powerful depressant of the spinal centres. To the former class belong the bromides, lobelia, and the more recently revived remedy, conium; while in the latter would be grouped arsenic, calabar bean, chloral, cimicifuga and antipyrin. Antipyrin alone reaches a little further in its action, and exerts upon the cerebral cortex a peculiar sedative influence.

In quinine, however, we have a remedy whose action upon the nerve centres differs radically from that of the remedies we have as yet mentioned. Since the researches of Chaperon, thirty-five years ago, repeated experiments in the physiological laboratory have abundantly demonstrated the soundness of his claims. The direct stimulating action of quinine upon the so called inhibitory centre of the cord, even in small doses, is now thoroughly established. Undoubtedly, during its exhibition there is a remarkable diminution in the reflex activity of the spinal centres. In cinchonized animals the discharges

of motor force are sensibly lessened, and this spinal inhibition increases *pari passu* with the degree and duration of the cinchonism. This interesting observation suggested to Professor Wood the possible utility of quinine in the chorea of dogs. A choreic animal in the Hospital of the Veterinary Department of the University of Pennsylvania was subjected to the method of treatment, and with a most interesting and satisfactory result. Within one week from the initial dose of quinine, as Professor Wood records, the spasmodic muscular movements had almost entirely disappeared. With this indication to its still further applicability in the management of convulsive spinal affections, choreic patients visiting the dispensary for nervous diseases in the University Hospital were placed upon the quinine treatment, under the direct supervision of Professor Wood and Dr. Potts. While the time that has elapsed since the commencement of the treatment has been short, and the number of patients limited, the results obtained thus far have been to say the least, gratifying. In but four instances did the disease fail to respond to the influence of the drug. A synopsis of the cases so treated is appended.

Case I.—L. C., aged 14, female. Is attending school. Family history good. Has had all the diseases of childhood, including scarlatina. Her first choreic attack was noticed on January 1, the twitchings beginning in the tongue. The movements at the time of her first visit, on the 19th of January, were general and severe. She had difficulty in talking, and at times bit her tongue. She was given quinine gr. iv, every three hours, until cinchonized, and then three times daily.

January 21. Movements still present, but much better.

February 24. Reports herself nearly well.

Case II.—M. A., aged 14 female. Attends school. Reported at the dispensary on the 9th of December, 1892, suffering with her second attack of chorea. The movements had begun a few days before, subsequent to a febrile attack. No history of rheumatism. The movements were general. She was placed upon increasing doses of Fowler's solution and iron, and this treatment was continued without marked benefit until February 11, 1893. She was then given quinine, gr. iv, four times a day, with immediate and considerable improvement. She was under this treatment for ten days, at the expiration of which time she reported herself as cured.

Case III.—E. F., aged 8, female. Attends school. Reported first at dispensary March 14, 1893.

The choreic movements had been noticed since the 1st of January, the attack having followed a fright. They began in the left arm, and at the time of her visit the entire left side was affected. Her speech

was thick; she complained of pain in her left knee, and her mother said that she had enuresis since the chorea began, although perfectly healthy previous to this. The family history was good. She was placed upon quinine, gr. iv, four times a day.

March 17. Reports much better, and did not return. The presumption is that she was cured.

CASE IV.—L. D., aged 10, female. Attends school.

February 24. Visited the dispensary with the second attack of chorea, which had lasted then for about a week. The movements were confined to the right side. No rheumatism. Was given quinine, gr. iv, four times daily.

February 27. Mother reports great improvement.

March 13. No movements noticeable.

April 5 Return of some movements. The quinine was continued and syr. ferri iodid., gtt. iii, and emul. ol. morrhuæ, f℥i, t. i. d., were added to the treatment.

April 19. Reported with complete disappearance of the choreic movements.

CASE V.—L. K., aged 14 years. School girl.

March 1, 1893 Came to the dispensary with slight choreic movements, affecting principally the muscles of the face. This is her second attack, the first one occurring when a year old, and lasting for three years. She was ordered quinine, gr. iv, four times daily.

March 13. Her mother reports that she is much better. Cinchonism present.

May 1. Came back with return of symptoms, which she says commenced soon after stopping the medicine. The same treatment as before ordered was advised, and at this date, May 17, 1893, she has not returned.

CASE VI.—M. H., aged 9, female. Attends school.

November 7, 1892. First visit, the attack being of two weeks' duration. The movements began on the left side, which is now the worse, though both sides are affected. No history of rheumatism or other acute diseases. Has always been nervous. Heart's action rapid. Was placed on increasing doses of Fowler's solution without improvement.

December 6. Is taking ten drops of Fowler's solution with compound syrup of the hypophosphites. Some gastric irritation present

December 19. Considerable irritation. The dose was reduced to drops v.

January 25. Choreic movements somewhat better, but has developed a neuritis in both legs. Was given quinine, gr. iv, t. i. d.

February 8. Choreic movements have nearly disappeared. Has not completely regained the power in her legs, but they are much improved.

February 21. No evidence of chorea visible.

CASE VII.—D. K., aged 12 years. Male. Attends school and works on a farm between times. Visited the dispensary April 12, 1893, suffering from his first attack of chorea. The movements were very severe, involving both sides; he could feed himself only with difficulty, and his speech was so much affected that it was almost impossible to understand him. Quinine, gr. iv, four times daily was ordered.

April 15. No better. Dose increased to gr. iv, five times daily.

April 17. No improvement. Increased to gr. vi, q. i. d.

April 21. About the same. Ordered Fowler's solution, gtt. iii, t. i. d.

April 26. Somewhat better. Is taking five drops of Fowler's, t. i. d.

May 11. Is nearly well. Fowler's solution, gtt. x, t. i. d.

CASE VIII.—R. B., aged 11 years, female. Attends school. Was treated at the dispensary for her first attack of chorea, from April 26, 1892, to August 9, 1892, with arsenic and tonics. No movements when she stopped treatment. Returned March 14, 1893, with slight movements. Was given quinine, gr. iii, five times a day.

March 17. Reported worse.

April 7. No improvement, when she was again placed on Fowler's solution, gtt. iv, t. i. d.

April 17. Much better. Is taking gtt. vii, of Fowler's solution.

May 2. Not so well. Fowler's solution was increased to gtt. ix, t. i. d.

She has not returned at this date, May 17, 1893.

CASE IX.—M. C., aged 14 years. School girl.

April 10, 1893. Returned to the dispensary with her second attack of chorea, her first one occurring about one year ago. The present attack has lasted several months. Both sides and speech affected. Ordered quinine, gr. iv, four times daily.

April 13. Seems considerably better. The dose of quinine increased to gr. iv, five times a day.

April 21. Choreic movements have almost disappeared.

May 16. Return of some movements involving principally the hands.

CASE X.—M. D., aged 7. Admitted to the hospital suffering with marked chorea of several weeks' duration. Gait very unsteady, almost staggering. Unable to feed herself. Was placed upon Fowler's solution for one week with but slight improvement. Three grains of quinine were then given in solution, five times a day. In three days there was a very perceptible diminution in the choreic movements.

In two weeks she was able to use her hands in eating; in another week the choreic tremor was no longer noticeable. With the improvement in this respect there occurred also a change in her disposition, the child becoming brighter and more playful. Fifteen grains of quinine were administered daily for three weeks without the slightest sign of cinchonism. Appetite remained good throughout.

CASE XI.—M. B., aged 12. School girl.

May 16, 1893. Second attack. Slight chorea for one week, preceded by rheumatic pains. Was given quinine sulph., gr. iv, q. i. d.

May 22. Chorea worse, gr. vi, t. i. d. Pil. iron and strych., t. i. d.

May 25. No improvement. Fowler's solution, gtt. iv, t. i. d. Has not reported since.

CASE XII.—A. L., aged 14. School girl.

May 15, 1893. Chorea since March, both sides and speech affected. Mother has had convulsions of an epileptic character. Was given quinine sulph., gr. vi, t. i. d.

May 22. Better, gr. vi, t. i. d., and pil. of iron and strych., t. i. d.

May 29. Much better. Is taking quinine, gr. xxvii, daily.

CASE XIII.—M. A., aged 12. School girl.

May 13, 1893. Second attack, first one in 1892. Movements in left side of moderate severity and do not cease during sleep. Was given quinine, gr. iii, t. i. d.

May 17. No better, gr. vi, q. i. d. Strych. sulph., gr. $\frac{1}{60}$, t. i. d.

May 20. About the same. Was given Fowler's solution, gtt. iv, t. i. d.

May 24. No better; dose of the Fowler's solution increased to gtt. v.

May 29. Slight improvement.

CASE XIV.—C. S., aged 14. Salesgirl.

May 13, 1893 More or less choreic movements of muscles of face for past four years. Lately these have involved entire body. Was given quinine sulph., gr. vi, t. i. d.

May 17. No better, gr. vi, q. i. d.

May 19. Much better. Syr. hypophos. co., ℥j, t. i. d.

May 27. No chorea.

CASE XV.—D. R., colored, aged 10. School boy.

May 24. Has had choreic movements for one year, which of late are much worse; both sides and speech now affected. Was given quinine sulph., gr. iv, t. i. d.

May 29. Better, gr. iv, t. i. d., and pil. iron and strych.

CASE XVI —Notes given by Dr. Lawrence S. Smith, Resident Physician, University Hospital.

J. F., aged 10. School girl. Born in England; one of three children. One sister is feeble minded; another is weak and delicate.

Two or three years ago she was frightened by a dog, and to this occurrence her mother attributes the chorea which began at that time, and has continued with increasing severity. When admitted to the hospital on February 3, 1893 the choreic movements were almost constant, and so violent that she was not able to articulate distinctly, to feed herself, or to walk without great staggering and imminent danger of falling. She was much emaciated, appetite very poor, and she appeared almost feeble minded. She was given quinine sulph., gr. iii, in solution, six times in the day, and this was borne without any unpleasant symptoms.

The dose was increased to gr. vii, three times daily, in about a week, and again in seven days to gr. vii, four times a day. With this increase in the dose, emulsion of cod liver oil, f℥ii, t. i. d., was ordered. The quinine and cod liver oil did not affect her stomach, and she complained of no unpleasant symptoms.

Under this treatment she gained in weight, her appetite doubled and her mental condition improved. The choreic movements became very much less violent within three days after she was placed under treatment, and they continued to improve while she was in the hospital. She could talk, eat and play around like other children, and at times the chorea was scarcely noticeable. From being almost helpless she became as active, jolly and useful as any of the children in the house. She was discharged improved April 15, 1893; since she left the hospital she has not been heard from.

Case XVII.—T. De A., aged 15 years, school girl, was admitted to the hospital on June 1 with her fourth attack of chorea. She has always been nervous, and from infancy has suffered with enuresis. The present attack is of one month's duration, the movements involving the left side. She is unable to hold anything in her left hand; speech is slightly involved. She was given quinine sulph., gr. vi, five times daily.

June 5. Reports better. Was given syr. hypophos. co., ℥i, t. i. d.

June 9. Is able to hold things much better. The dose of quinine now increased to gr. vi, six times daily.

June 14. Much better. A curious fact is that she has not wet the bed since taking the quinine. She is now taking forty grains daily, and there is no cinchonism.

June 19. Reports almost cured.

In addition to these, several severe cases were placed upon this treatment by Dr. J. H. Musser, who kindly sends us the following summary of his results: "They all bore enormous doses of quinine with benefit at first, but subsequently relapses took place, and final cure ensued after the use of arsenic."

This record must be left to speak for itself. It will be noticed that in a number of the cases almost immediate improvement took place, which continued for a time, after which relapses occurred. This occurrence, it seems to us, may be due to the fact that the quinine merely acts as a stimulant, and like all stimulants loses its effect in time, to be followed by depression. Therefore, so far as any conclusion can be drawn from such a limited number of cases, it would seem that the best treatment for chorea would be the administration of large doses of quinine to lessen the severity of the movements, adding at the same time measures to build up and strengthen the depressed nervous system. This seems to be shown in Case IV, where final cure only took place after the administration of cod liver oil and iron, and also in Case X, where cod liver oil also had to be administered after a time. Another fact worthy of emphasis is the large doses that the majority of the children could take without any evidence of cinchonism. Finally, we do not claim that quinine is an absolute cure for chorea, and that from this time no such thing as failure in the treatment of such cases will be recorded. It should be borne in mind that after the chorea has been of long standing, and the loss of inhibitory power considerable or absolute, there must result organic changes in the motor cells of the cord, with the development of an atrophic condition. In such cases it is probable that failure will be the result of any form of medication, however rational. What is claimed is that in the acute form of chorea the results thus far obtained from the administration of quinine in large doses have been such as to warrant a further investigation as to the merits, immediate and ultimate, of this line of treatment.