THE USE OF STRAMONIUM FOR THE RIGIDITY AND DROWSINESS FOLLOWING ENCEPHALITIS LETHARGICA

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THE use of stramonium in post-encephalitic conditions, especially for Parkinsonian rigidity and mental apathy, has not received the attention it deserves from the medical profession. With a daily dose of stramonium the patient's life may be rendered comparatively happy. With it, he may be enabled to accomplish the fundamental necessities of life, to walk, dress and feed himself, to write and even to earn his own living. Without it, the patient may be compelled to drag out a crippled and sleepy existence with his daily wants falling as a burden on others. The stramonium must be given continuously in large doses, *e.g.*, half a drachm of the tincture thrice daily. At the West Park Mental Hospital, London, many cases of post-encephalitic Parkinsonism are cared for. Most of these patients are kept on substantial doses of the stramonium tincture for many years. If the stramonium be withheld it is found that the patients rapidly relapse to their former pitiable condition. Stramonium is also in common and satisfactory use throughout the British mental and general hospitals.

The history of introduction of stramonium is of interest. In 1895, Erb discovered the calming effect of hyoscine injections for the tremors of paralysis agitans (senile Parkinsonism). About 1914, Dr. Arthur Hurst noted that larger doses of hyoscine could be given with greater benefit and the toxic effects which would otherwise ensue prevented by adding pilocarpine to the hyoscine injections.

When it was found that the Parkinsonian syndrome frequently followed encephalitis lethargica, it was only natural that hyoscine should be tried in this condition also. Quite unexpectedly however hyoscine was found to have little or no effect on the tremor which is generally much less pronounced than in senile paralysis agitans, but on the other hand was found to exert a very favourable influence on the rigidity following encephalitis lethargica, whereas the rigidity of paralysis agitans remains completely unaffected by hyoscine. In 1926, stramonium was found even more effective than hyoscine in relieving rigidity, slow movement and salivation. The mental, as well as the physical, condition of the patient was also profoundly affected. In 1928, Hurst suggested prescribing pilocarpine with larger doses of stramonium to avoid overdose symptoms of dry mouth, vomiting, and of accommodation paralysis. The result has been most satisfactory and in every case improvement has been shown and at times the whole existence of the patient has been profoundly modified as in the case quoted below.

Mode of action of stramonium.—The nerve centres controlling tone are situated at the base of the brain in the corpus striatum and in the substantia nigra of the crura cerebri. The centres are in turn controlled by impulses from higher centres. Injury to them, as in Parkinsonism, results in excessive tone (rigidity) in the voluntary skeletal muscles. Stramonium contains hyoscyamine, hyoscine and atropine. Drugs of this series abolish the tone of involuntary muscles by paralysing the parasympathetic, *vide* their effect in asthma, but have no action on motor nerves. The injection of cocaine in paralysis agitans abolishes the rigidity by paralysing the sensory nerve endings. Atropine applied locally also paralyses sensory nerve endings, but when given by the mouth it is not considered to have local action. Nevertheless, stramonium by the mouth abolishes post-encephalitic rigidity.

A case of post-encephalitic Parkinsonism

K., a single male, aged 25 years, vegetarian, was admitted on 17th October, 1934, into my ward in King George's Hospital, complaining of (1) weakness and rigidity in both legs with inability to walk, (2) a similar condition in both arms and in the head and the neck, (3) drowsiness by day and insomnia by night, all for the past three months, and (4) excessive salivation for two weeks.

History of present illness.—Nine months back the patient set out from Travancore on a pilgrimage to Rishikesh, which he reached in 14 days and where he lived with Sadhus for five months. During this period he was quite healthy. About three months ago, he got fever which lasted for a few hours and was accompanied by slight shivering. The following day he had a second attack of fever for a similar period. This intermittent type of fever continued for 10 days. He lost his appetite and sleep and became constipated. There was no history of headache, hiccough, vomiting, diplopia, or ptosis, nor of incontinence, but occasional

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Linton, R. W., Mitra, B. N., and Seal, S. C. (1935). *Indian Journ. Med. Res.*, Vol. XXII, p. 617.
Linton, R. W., and Seal, S. C. (1935). *Indian Med. Gaz.*, Vol. LXX, p. 68.
Linton, R. W., Shrivastava, D. L., and Mitra, B. N. (1935). *Indian Journ. Med. Res.*, Vol. XXII, p. 633.
Pasricha, C. L. (1934). *Annual Report, Calcutta School of Tropical Medicine*, 1933, p. 37, Superintendent, Government Printing, Bengal.
Pasricha, C. L., DeMonte, A. J., and Gupta, S. K. (1931). *Indian Med. Gaz.*, Vol. LXVI, p. 610.
Pasricha, C. L., DeMonte, A. J., and Gupta, S. K. (1932). *Ibid.*, Vol. LXVII, p. 487.
van Loghem, J. J. (1913). *Centralbl. Bakt.*, Abt. I, Orig., Vol. LXX, p. 70.
Wherry, W. B. (1904). *Pub. No.* 19, *Bureau Govt. Lab.*, Washington, U. S. A.
Zimmermann, E. (1934). *Brit. Med. Journ.*, Vol. II, Epitome, *Current Med. Lit.*, p. 60.

incontinence was observed after his admission to hospital. A few days after the fever, the patient appears certain (though his memory is definitely impaired) that he noticed slight weakness in his right arm; then his left arm became weak; then his head and neck; then both legs at the same time; and within a month he could only hobble, all bent and stiff, with the help of a stick. There is no history of any important illness nor of exposure to venereal disease.

Clinical condition on admission.—The patient lies quiet and drowsy in bed, mostly on his left side with the knee drawn up (figure 1). He

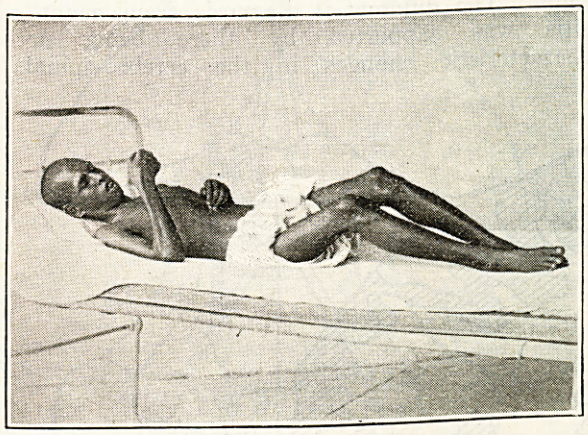

Fig. 1.

pays no attention to what is passing round him. The left position is maintained since owing to the weakness and drowsiness considerable difficulty is experienced in turning over. The patient can be readily roused from his stupor if shaken or spoken to sharply, but rapidly becomes apathetic again. He is unable to dress himself and does not ask for food, but will stretch out his hand to take food if he is told to and the food is placed near him. He cannot write, though formerly he did so. He does not leave his bed for defæcation, nor to pass urine, but usually calls the ward boy in good time. Occasionally incontinence is present. His body is thin. His face is immobile and mask-like. His head is moved little and his neck is rigid. When his attention is attracted by a noise at one side he turns his eyes in that direction first and not his head. His head, neck and vertebral column move as though they were connected in one piece by a rod of iron. All his movements are laborious, stiff and slow. Mentally he is decidedly dull. He takes long to understand and to reply to questions (slow cerebration). He speaks very slowly. His memory is markedly impaired. Though by day he is always drowsy yet he complains of insomnia and his sleep was much disturbed. Occasionally his eyes deviate outwards and remain fixed for a few seconds (third and sixth nerves) and then float inward again (oculogyric crises). On closing his eyes, both eyelids quiver rapidly in recurring rhythmic movements. His lips are frequently pursed together. On making an effort to talk his lips also vibrate rapidly (seventh nerve). When he protrudes his tongue, marked fine tremors are noticed (twelfth nerve). He frequently opens his mouth slowly and closes it again (fifth nerve). Dribbling of saliva from the corners of the mouth is present (bulbar involvement). There is no squint, no ptosis and no diplopia. The left

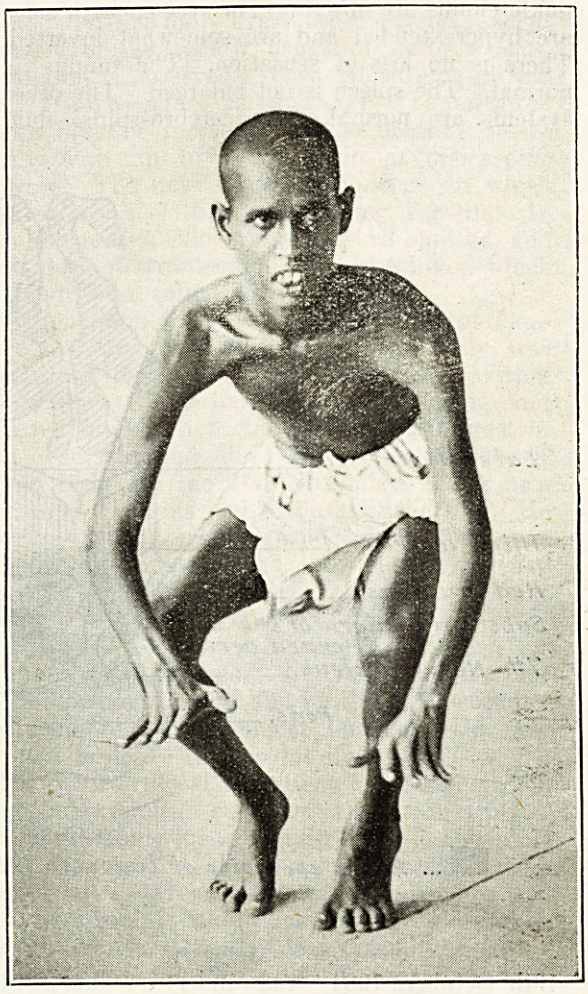

Fig. 2.

seventh nerve is definitely weak, from a nuclear lesion as the forehead wrinkles normally. He does not voluntarily sit up in bed, much less stand or walk. When forced to walk he can only do so very slowly, stiffly and with the greatest difficulty. His shoulders are round and bent forwards and so is his body at the waist. Both upper and lower extremities are weak and spastic, but the right arm is more spastic than the left. The right upper extremity is held semi-pronated, flexed at the elbow, adducted, and with slight ulnar deviation at the wrist. The fingers are partially flexed at the

metacarpo-phalangeal and at the inter-phalangeal joints. The thumb is adducted and flexed over the index finger as in paralysis agitans except that thumb and finger tremors are absent. The patient cannot voluntarily extend his fingers. The grip is impaired. The biceps, triceps and supinator reflexes are brisk on both sides. The abdominal reflexes are present. In the lower extremities, the stiffness is marked, especially on the right. Reflexes on both sides are brisk, more so on the right (tendency to right-sided involvement). Babinski's sign and ankle clonus are absent. The feet on both sides are hyperextended and are somewhat inverted. There is no loss of sensation. The fundus is normal. The spleen is not enlarged. The other systems are normal. The cerebro-spinal fluid (19th October, 1934) was under no increased pressure; 15 c.cm. were withdrawn. Eight cells (mostly lymphocytes) were counted per c.mm., the albumin was 2 per cent, chlorides 67 per cent, and sugar 1 per cent. The Wassermann reaction of the blood and of the cerebro-spinal fluid was completely negative.

On the 17th October, 1934, the day of his admission, the patient's temperature was 105°F. falling to normal and again rising to 102°F. on the 18th October. After the 18th the temperature remained normal for three days when it became definitely tertian for three paroxysms. Though on the 19th October the blood report was negative to malarial parasites, yet the clinical diagnosis of malaria being established, the fever was controlled with quinine, atebrin and plasmochin.

Diagnosis.—The rousable lethargy, the oculogyric crises, the Parkinsonian-like rigidity, the spontaneous involuntary movements in the opening and closing of the lower jaw, with the eyelid, lip and tongue tremors and occasional incontinence left little doubt that the patient was in the chronic stage of encephalitis lethargica.

On the 20th December, the cerebro-spinal fluid showed the following results :—Wassermann reaction—completely negative, albumin—0.15 per cent, no organisms, and two cells per c.mm. The differential diagnosis from meningitis was supported by there being no characteristic changes in the cerebro-spinal fluid, from poliomyelitis by the absence of any sign of lower motor neuron lesion, from crossed paralysis due to a tumour or vascular lesion in the pons by the onset of the disease with fever and without signs of any rise in intracranial pressure, as shown by the normal fundus and normal pressure; and finally from syphilitic cerebral lesion by the absence of a positive Wassermann reaction in the blood and in the cerebro-spinal fluid.

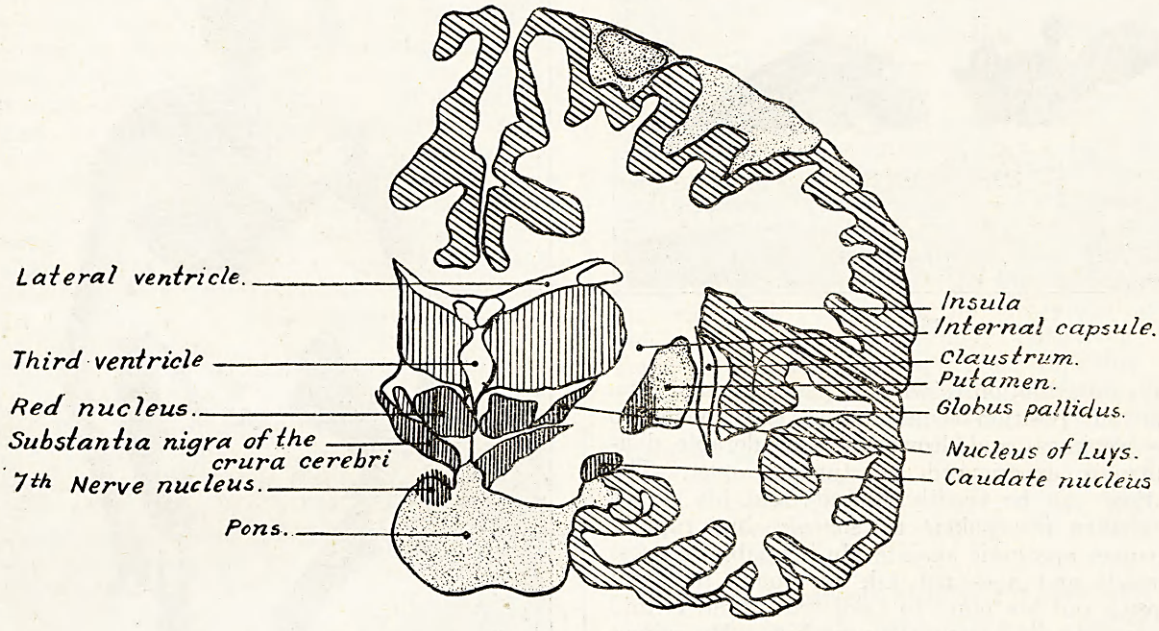

Fig. 3.

Pathology.—In encephalitis lethargica the grey matter of the cortex and of the basal nuclei is rosy pink from inflammation, whilst the white matter is not involved. In the rigidity and the tremors of post-encephalitic lethargica, as in paralysis agitans, the motor

cells in the grey matter of the substantia nigra of the crura cerebri, in the grey matter of the corpus striatum (caudate nucleus and globus pallidus of the lentiform nucleus), and in the grey matter of the subthalamic region (red nucleus and nucleus of Luys) are especially involved. The typical symptoms produced are rigidity, tremors, slow and weak voluntary muscular contractions, and spontaneous involuntary movements. The mental lethargy is probably due to involvement of the cerebral

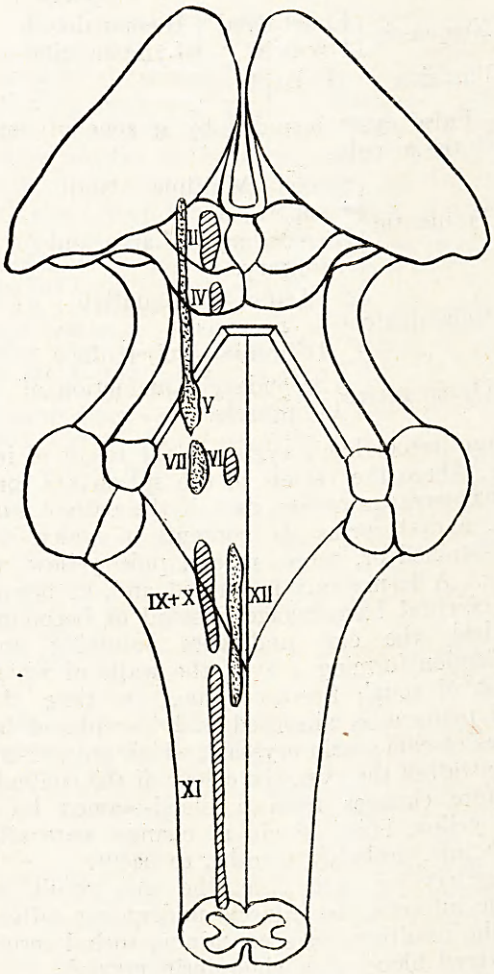

Diagram showing motor nuclei

▒▒ ... *Nuclei affected.*

Fig. 4.

In the case quoted, the fifth (temporal and masseter muscles), the seventh (eyelids, lips and tremors) and the twelfth nuclei (the tongue tremors) were affected.

cortex. The left facial paralysis, with increased rigidity of the right side of the body, was a crossed hemiplegic manifestation arising from a lesion especially developed in the upper part of the left pons—where the face nucleus for the same side is (*see* diagram). The eyelid, lip, tongue and jaw tremors are due to involvement of the fifth, seventh and twelfth nuclei in the floor of the fourth ventricle.

Treatment

The modern treatment of post-encephalitic Parkinsonism follows three distinct lines :—(1) stramonium, (2) physical drill, and (3) psychotherapy.

Method of giving stramonium.—A start is made with 30 minims of the tincture of stramonium in half an ounce of water thrice daily after meals. Five minims of the tincture is added thrice daily every other day until slight dryness of the mouth or paralysis of accommodation is observed. Then pilocarpine nitrate gr. 1/10th is added to each dose. The stramonium may be increased to one drachm thrice daily with up to 2/5th grain of pilocarpine nitrate. The dose of the two drugs on which the patient feels best is continued for life. In the alternative, pilocarpine may be omitted, and that dose of stramonium only determined which is found best suited to the patient.

Stramonium treatment of this patient.—Tincture of stramonium, 30 minims thrice daily, was prescribed from 16th November, 1934. Within three days the lethargy was diminishing and the patient began to take far more interest in the events around him. He commenced to sit up in bed. On the 21st November, of his own accord, he left his bed to bask in the sun. He started to walk around, which he had not done for the last four months. On this day, a five minutes' walk was prescribed four times daily as part of his treatment. On the 28th November he was able to feed himself and asked for the food delicacies he liked. On the 2nd December he dressed himself and on the 3rd December he went to the bathroom unaided. He now started to desire to earn his living.

Physical drill.—The patient was instructed in physical exercise, such as rising on tip-toe, whilst extending his arm and raising it above his head (figure 2). Later, he was prescribed more complicated exercises and was re-taught to run. The number of times each exercise was to be performed was definitely laid down.

Psychotherapy.—The patient was improving mentally as well as physically. He felt the change in himself, and was very happy. Every morning he would tell the doctor, the students and the nurses that he was feeling much stronger. He was encouraged and praised at every success, he was given tumblers of water to carry about the ward, and some useful light ward duties. He massaged himself with oil with the twofold purpose, that mechanical movement and massage were good for him, and that active mental effort was initiated. The patient was thus encouraged to work for himself and for others as much as possible. Cerebral re-education, physical and mental, was helped in every possible way.