CASE OF TETANUS TREATED WITH DECAMETHONIUM IODIDE

BY

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In the treatment of tetanus the efficacy of muscle relaxants in preventing exhaustion of the patient from excessive muscular activity has already been shown. Curare has been used by several workers (Hoche, 1894; Cole, 1934; Mitchell, 1935; West, 1936; Cullen and Quinn, 1943; Adriani and Ochsner, 1947; Ory and Grossman, 1948); more recently the use of "myanesin" (mephenesin) has been reported (Belfrage, 1947; Davison, 1949; Davison *et al.*, 1949). It may be of interest to report a case of tetanus in which the relaxant used was the much discussed bistrimethylammonium decane di-iodide (decamethonium iodide, or C10). There were four main reasons for the choice of C10: (1) Both D-tubocurarine chloride and "flaxedil" had been tried by the physicians in charge of the case, with the production of marked respiratory depression and profuse salivation. (2) Myanesin was considered, but, in view of its tendency to produce haemoglobinuria, was rejected. (3) Experience with C10 in anaesthesia has shown that adequate relaxation of the larger skeletal muscles could be achieved without profoundly depressing respiration, and without relaxing the pharyngeal muscles. (4) C10 has less power to liberate histamine than D-tubocurarine chloride and therefore to produce bronchospasm.

Case Report

A girl aged 19 was admitted to the Belfast City Hospital on April 28, 1950, with a history of trismus and severe backache for four days, and opisthotonos and spasms, with very severe pain since the previous day. Two weeks previously she had got a wooden splinter under her finger-nail.

On examination she was seen to be a healthy, well-nourished girl, with a typical risus sardonicus, moderate opisthotonos, and marked trismus—being unable to put out her tongue, and spasms lasting 20 seconds occurring every two minutes; between spasms the muscles were rigid. A clinical diagnosis of tetanus was made (unfortunately the splinter was thrown out with the soiled dressings and a piece of loose nail which separated), and the patient was treated with massive intravenous doses of A.T.S., penicillin, and sedatives. This treatment was successful at first, but spasms returned as soon as the effect of sedation lightened and she became restless.

On the third day small injections of curare in oil were tried, with no effect. Intravenous D-tubocurarine chloride was then tried in 10-mg. doses, and flaxedil in 40-mg. doses, both achieving profound relaxation with respiratory depression for periods of about 30 minutes, after which rigidity and spasms returned as before. The pulse rate and temperature remained high, and the patient's general condition was poor. The physicians in charge of the case decided to seek my opinion as an anaesthetist, and the following treatment was carried out.

On examination the patient was distressed, crying out with the pain of the spasms, flushed, and sweating profusely, and the muscles of the trunk and limbs were rigid. It was decided to try the effect of C10. At 11.45 a.m. on May 2 a slow intravenous injection of C10 was started, 1 mg. at a time. During half an hour 5 mg. was given, producing some relaxation and no respiratory depression. A further 3 mg. was given over the next 15 minutes. The respirations became shallow and cyanosis developed. The injection was stopped and the patient was turned on to her side with her head over the side of the bed, and oxygen was administered by mask. The pharynx filled

with sticky mucus, which was periodically swabbed out. She remained unconscious for one hour. The breathing then became noticeably deeper, and she opened her eyes. Fifteen minutes later she was sitting propped up, coughing, and blowing out mucus. After another 15 minutes 1 mg. of C10 was given intramuscularly with 50 mg. of pethidine intravenously and 50 mg. intramuscularly. She was then put in an oxygen tent at 2 p.m.

Small intramuscular doses of C10 and pethidine were given at 7 p.m. and the patient remained comfortable until 9.45 p.m., apart from slight tremors which were seen mainly on effort. Spasms then returned, and a further intravenous injection of 2 mg. of C10 with 50 mg. of pethidine was given, followed by the same dose intramuscularly. An extract from the notes summarizes the effect of these injections. "10 p.m.: Patient restless, crying out, tearful, and frightened. After injection: Quiet, rational, grateful."

In 48 hours 50 mg. of C10 and 950 mg. of pethidine were given. Spasms returned as the effect of the injections wore off, but were easily controlled, and the patient's general condition was much improved. On the evening of the third day of treatment her temperature rose and coarse crepitations were heard at the left lung base. C10 was withheld and a course of streptomycin started. She was encouraged to cough, and postural drainage, with deep percussion, was instituted. With the energetic co-operation of patient and nursing staff the chest was cleared in less than 24 hours. During this time it was necessary to increase the dosage of pethidine to 600 mg. a day. Pain was fairly well controlled, but spasms were troublesome and sleep was disturbed.

After this incident 1/100 gr. (0.65 mg.) of atropine was given six-hourly to cut down secretions. Treatment with C10 was restarted and continued for a further five days, dosage and frequency being judged by the response of the patient. The usual requirement was 2-3 mg. every four to five hours. It was found that, even with the large amounts of pethidine being given, a soporific was necessary at night. The chest remained clear, the spasms became less frequent and less severe, and her general condition improved.

On the evening of the tenth day of the treatment (the fourteenth day since admission) it was noticed that the occasional spasms now coincided with the appearance of the medical attendants. We came to the conclusion that the patient had probably

Chart showing dosage. PN = Penicillin. SM = Streptomycin.

developed a mild addiction to pethidine. Paraldehyde, 4 mg., was given intramuscularly. This raised a storm of tearful protest, but the patient slept soundly and no further spasms were seen. On May 15 she was up in a chair, and on May 23 walked with assistance. The muscles were still sore and stiff, but recovery was helped by physiotherapy. She was discharged on June 8.

The total dose of C10 was 135 mg., representing a daily average of 15 mg., and of pethidine 4,230 mg., with a daily average of 470 mg. The distribution is shown in the Chart.

Discussion

The treatment of tetanus with relaxants is not curative. It is still necessary to give A.T.S. and penicillin in massive doses and to build up the patient's general resistance. The experience gained in the treatment of this case, together with a study of the literature, enables certain general principles to be stated.

Sleep.—Even when painful spasms are abolished there may be a fair amount of residual pain from aching and torn muscles, so that an analgesic must be prescribed as well as sedatives to ensure sufficient sleep.

Secretions.—It is futile to abolish the spasms of tetanus, only to let the patient drown in his own secretions. Atropine is useful to cut down secretion. The cough reflex must not be dulled by sedatives, and the patient must be encouraged to cough. If necessary, curarization must be lessened to enable the patient to cough.

Oxygen.—Adequate oxygenation must be ensured. Anoxaemia increases the permeability of the capillaries in the lungs, allowing fluid to escape into the alveoli. If respiratory depression is present, oxygen must be administered. It is suggested that if adequate ventilation cannot be maintained by other means the patient might be nursed in an iron lung.

Nutrition.—Feeding presents no difficulty, since with C10 the patient is usually able to swallow. If, however, the effort proves exhausting, a fine plastic tube, as recommended by Bull *et al.* (1949), can be passed into the stomach with remarkable ease.

Fluids.—Fluid intake and output should be checked and an adequate balance maintained. If the temperature is high, much fluid may be lost by sweating and through the lungs. Haemoconcentration should be watched for by repeated haemoglobin estimations. Urinary chlorides should be estimated and any deficiency made good.

There should always be available a supply of oxygen, with a facepiece and reservoir bag, a mouth gag, tongue forceps, a sucker, and a supply of gauze wipes, a laryngoscope, and endotracheal tubes.

Comparison with Other Relaxants

The causes of failure with curare in the treatment of tetanus are the inadequate margin between the lissive dose and that causing respiratory paralysis, bronchial spasm, and accumulation of secretions.

Myanesin seems to have none of the disadvantages of curare. It has, however, two of its own: a tendency to cause venous thrombosis at the site of injection, and the production of haemoglobinuria. Davison (1949) makes out a very good case for the use of this drug in tetanus. He points out that proof of haemoglobinuria is lacking, since the breakdown products of the drug may produce a positive reaction to the benzidine and guaiac tests, and, further, that in no case has the so-called haemoglobinuria been shown to have any adverse effect on the patient.

C10 has the disadvantages of neither curare nor myanesin. In the above case, on only one occasion was respiration

depressed to such an extent as to require inflation of the lungs with oxygen. This occurred with a very large dose—9 mg.—given initially. It is of interest to note that this amount was required to produce relaxation after two intravenous injections of 5 mg. of D-tubocurarine chloride had been given 50 minutes and 1 hour previously. This confirms the experimental finding of Paton and Zaimis (1948) that, although the potency of D-tubocurarine is not affected by the previous administration of C10, twice as much C10 is required after a previous dose of D-tubocurarine. Subsequently, the dosage averaged 2–4 mg. at three- to four-hourly intervals. On one occasion 5 mg. was given, but this dose paralysed the intercostals, and, though no cyanosis was seen, the patient was put in the oxygen tent.

West (1936) expressed the opinion that the development of bronchial spasm was a very real danger in the use of curare. The occurrence of this complication is probably less likely with the pure D-tubocurarine chloride now available, but even with this material it is still seen fairly often. Paton and Zaimis (1948) found that the power of C10 to liberate histamine was one-quarter that of an equivalent dose of D-tubocurarine. This leaves an adequate margin of safety.

Accumulation of mucus was seen after the first dose of C10, and on the third day there were signs of fluid at the base of the left lung. Otherwise there was no trouble with excessive secretion. Coughing and swallowing were possible throughout the treatment. I feel that the choice of analgesic helped to achieve this result.

Pethidine is structurally related to atropine, and has mild atropine-like properties (Batterman and Himmelsbach, 1943). In addition to its analgesic and sedative action, it has, in contrast to morphine, an antispasmodic effect on smooth muscle, including bronchial musculature, and causes very little depression of respiration or of the cough reflex. Despite the enormous amount given, no ill effects were seen, and there were no withdrawal symptoms.

Summary

A case of tetanus treated with C10 and pethidine is presented.

It was found possible with these two drugs to control the spasms, abolish the rigidity, and relieve the pain of tetanus without unduly depressing either respiration or the cough reflex.

The advantages of pethidine as an adjuvant to the relaxant treatment are commented on.

The case is reported in the hope that others may be encouraged to give C10 a further trial. I should be interested to hear of any other cases.

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