

TREATMENT OF TWO CASES OF TETANUS WITH D-TUBOCURARINE CHLORIDE IN PEANUT OIL WITH MYRICIN *

GRACE G. BINGER, M.D., AND G. DEVNICH, M.D.

San Jose, California

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INTRODUCTION

OF the 21 cases of tetanus occurring at the Santa Clara County Hospital between January 1935 and January 1948, 65 per cent of the patients died. Since January 1948 we have had 2 more cases of tetanus and these patients were treated with d-tubocurarine chloride in peanut oil with myricin. We wish to report the results of this treatment.

HISTORY

As early as 1858 to 1861 T. Spencer Wells (1) reported 3 cases of tetanus in which the patients were treated with "Woorare."

In 1867 Busch (2) reported treating 21 cases of tetanus from the Bohemian War. Of these, 11 were given curare subcutaneously; 5 died and 6 recovered. He believed that curare was of aid in 5 of the patients who recovered. Busch also reported that Demme administered curare to 22 patients with tetanus and 8 recovered.

Since then numerous workers have used curare and intocostin subcutaneously, intramuscularly and intravenously in patients with tetanus. The results, on the whole, have been disappointing. Briefly, some of the reports follow.

In 1935 Cole (3) reported the survival of one out of 4 patients with tetanus. His treatment included the use of intravenous curare.

In 1935 Mitchell (4) used a curare preparation subcutaneously in one case of tetanus, with successful results.

West (5) in 1936 published the results of the use of a continuous intravenous drip of curarine in the treatment of 10 patients with tetanus; one patient survived.

Isacson and Swenson (6) in 1941 treated a child with tetanus using aqueous curare intravenously and finally intramuscularly, but the child choked to death on regurgitated vomitus.

Cullen and Quinn (7) in 1943 used intocostin intravenously and

* Since writing this paper we have successfully treated 2 additional consecutive cases of tetanus with d-tubocurarine chloride in peanut oil with myricin, bringing the total cases to 4.

intramuscularly in the treatment of 4 patients with tetanus, with one survival, a 43-year old man whose incubation period was four weeks.

Lundy et al. (8) in 1946 reported use of curare intravenously and intramuscularly in the treatment of a fatal case of tetanus in a child. They thought that sodium amytal given intravenously was of greater value.

Hanna (9) in 1946 reported the use of intocostin intravenously and intramuscularly in a case of tetanus, without survival. The patient, however, was in extremis before treatment was started.

Adriani and Ochsner (10) in 1947, used intocostin intravenously in 5 cases of tetanus, with survival of 4 patients.

Browne and Stone (11) in 1948, used intocostin intravenously and intramuscularly to treat a man with tetanus; the incubation period was twelve days. In addition to intocostin, antitetanus serum, benadryl, barbiturates and narcotics were used. The patient was able to leave the hospital fourteen days after entry.

Ory and Grossman (12) in 1948, successfully treated 2 patients with tetanus, using intocostin intravenously, with barbiturates and other drugs.

In addition to curare and its derivatives, dihydro-beta-erythroidine has been used *orally* by Goodman and Reinhardt (13) in the treatment of tetanus. This drug resembles curare derivatives in its muscle relaxant power. It is used in crystalline form and can be weighed accurately. They used it in a 33-year-old woman with postabortal tetanus and an incubation period of thirteen days. The initial dose was 20 mg. orally every hour and this dosage was gradually increased. They then stopped the drug for four days, with a return of convulsions. A total of 12 Gm. was given in twelve days. In addition, antitoxin, sedatives, and sulfadiazine were employed. The patient recovered and left the hospital in five weeks.

In 1947 Campos and Brazil (14) used a curare substitute, bebeerine dimethyl ether, with good results in 2 cases of tetanus. Muscular relaxation lasting two to three hours at a time was obtained.

Schlesinger (15) in 1946 reported use of d-tubocurarine chloride in oil and wax in 5 consecutive cases of severe tetanus, with no loss of life.

Since a patient who obtains relaxation with intocostin given intravenously or intramuscularly requires supervision by a physician twenty-four hours a day and still there is risk of tetanic asphyxia and paralytic asphyxia, or at least pneumonia from regurgitation owing to over-curarization, we were eager to try the curare preparation in oil and wax, given intramuscularly. We hoped that it would produce a more sustained, even relaxation than intocostin, given intravenously.

REPORT OF CASES

Case 1.—A 12-year-old boy was admitted to the Isolation Ward of the Santa Clara County Hospital at 7:20 p.m. March 18, 1948. Ten days before admission

a blister had developed on his heel from wearing new shoes. There was a purulent discharge from the blister seven days before hospital entry. He complained of backache for two days prior to entry.

On examination, the patient was unable to open his mouth. Examination revealed opisthotonos and trismus. The temperature was 100.6 F. rectally (the highest point it ever reached), pulse 100 and respirations 22. The blood count was normal. Urinalysis revealed a trace of albumin which subsequently disappeared.

Tetanus antitoxin was given intravenously, intramuscularly, and locally, benadryl being used because of a positive skin test.

Penicillin orally, mixed with saline and amphojel, was administered to avoid the stimulus of parenteral injection. Codeine was used for pain in the foot. Paraldehyde was administered rectally in the form of paraloids (each containing 5 cc. of paraldehyde) for one week before rectal irritation was noted. Atropine was used for excessive salivary secretion.

Debridement was done in the patient's bed with the least amount of stimulation possible. The procedure lasted fifteen minutes. Pentothal, 1.5 Gm., with 100 per cent oxygen and 70 units of intocostin intravenously was used.

d-Tubocurarine chloride in peanut oil with myricin was started March 21, 1948. One cubic centimeter of this preparation contains 27 mg. of d-tubocurarine chloride pentahydrate which is equivalent to 180 units of intocostin.* A dose of 0.5 cc. was given at 11:50 a.m. and at 7:20 p.m. on March 21; on March 22, 0.5 cc. was given four times and the same dosage at 2 a.m. March 23 at which time the supply of the drug was temporarily exhausted. The day the drug was started the patient had convulsions whenever touched and was incontinent. By 9:30 a.m. the next day he was able to have a bath without a convulsion. Respirations remained adequate. The patient's only complaints were occasional double vision and pain in the heel. By 8 p.m. on March 23 (the day the supply of the drug was exhausted) convulsions occurred again and he cried with generalized pain. At 11:30 a.m. March 24 he appeared to be in poor condition and was given 50 units of intocostin intravenously, with temporary relief. At 9:45 p.m. March 24 we secured more curare in oil. This was given in 0.5 cc. amounts at the time intervals noted on Chart 1 until April 4. The patient was discharged from the hospital April 8.

In a fifteen-day period the boy received 120 units of intocostin intravenously and 9 cc. of d-tubocurarine in oil, which is equivalent to 1740 units of intocostin.

The patient was never without a nurse in the room from the time the curare was started until the dose was decreased to once every forty-eight hours.

Case 2.—A boy, aged 10 years, entered the hospital May 10, 1948, complaining of neck pain and stiff jaws of two days' duration. He had pierced the left forearm with a fragment of bone from a decomposing cow one week before admission. The bone had been removed five days later by the mother because the area was discharging pus.

Physical examination revealed trismus, limitation of neck movement and hyperactive reflexes. The urine contained leukocytes, casts, and acetone on several occasions but finally cleared.

The wound was debrided the day of entry. Pentothal, oxygen and 20 units of intocostin intravenously were given. Considerable local tetanus was en-

* The drug was furnished by E. R. Squibb & Sons.

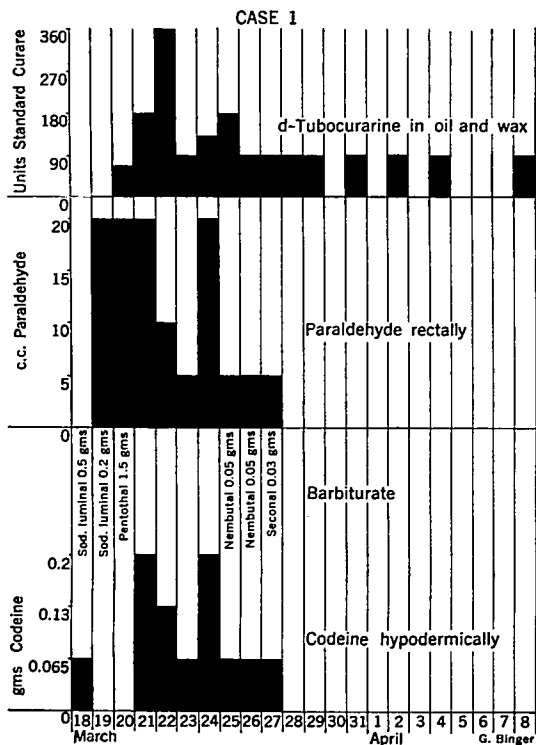


CHART 1.

countered. Subsequent culture of this debrided tissue revealed pure cultures of *Cl. tetani*.

The day of entry curare in oil was started in 0.25 cc. doses at four hour intervals. Symptoms progressed and the dose was changed to 0.5 cc. every four hours the following night. Opisthotonos persisted and spasm caused several near fatal asphyxial attacks. On May 16 the dose was changed to 0.75 cc. Nothing was ordered by mouth, but the night of May 17 when water was given to moisten the lips aspiration and asphyxia resulted, requiring nasotracheal intubation with oxygen insufflation. It was decided the patient was over-curarized and had suffered loss of power of deglutition. Curare was stopped; the last dose, 0.75 cc. was given at 2 a.m. May 18. By the night of May 18 the patient was again rigid and having convulsions with the slightest stimulus. A tracheotomy was done to prevent asphyxia. Curare in oil was started again at

2 a.m. May 19. From this point on the boy began to improve steadily. On June 2 administration of the drug was stopped. The tracheotomy was closed before he left the hospital.

This patient received a total of 20 units of intocostrin intravenously and 29.5 cc. of curare in oil intramuscularly in twenty-three days. He therefore received intocostrin equivalent of 5310 units (29.5 cc. times 180) in the form of curare in oil, plus 20 units of intocostrin. The complete record of dosage of curare is shown in Chart 2.

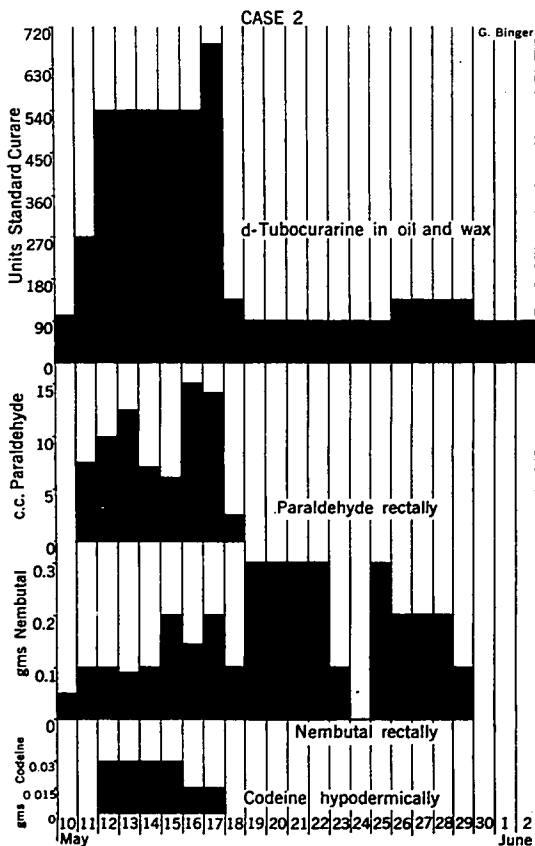


CHART 2.

In addition, the patient received 240,500 units of tetanus antitoxin, penicillin, benadryl, atropine and codeine. Barbiturates and paraldehyde were also used; an effort was made to concentrate them at night for their sleep-producing effect and to produce relaxation *with consciousness remaining* during the day by means of the curare in oil.

DISCUSSION

Curare in oil was of value in these 2 cases. The patients not only survived but they required a shorter period of hospitalization and left the hospital with fewer residual symptoms than the previous patients who recovered. The previous average hospitalization of patients who recovered was twenty-eight days and that of these patients was twenty-three and a half days.

We did not attempt to supplant the commonly used sedatives and hypnotics with curare. They were used at night to induce sleep. During the day curare was relied on for relief of convulsions, rigidity and generalized pain owing to muscle spasm. The patient was conscious and so could eat, urinate, defecate and move about. Codeine or other narcotic drug is still necessary if there is traumatic pain at a site of debridement. Atropine was helpful in preventing salivary secretion.

As to dosages, Schlesinger (15) pointed out that they are related more to degree of motor acceleration than to body weight, and duration of clinical effect seems inversely proportionate to degree of abnormal motor activity. Case 1, a large boy of 12, received the intocostin equivalent of 1740 units in fifteen days. Case 2, a small boy of 10 who had a more severe case of tetanus, received the intocostin equivalent of 5310 units in twenty-three days.

The instructions and warnings on each bottle of the drug relative to the administration of d-tubocurarine chloride must be followed exactly. The drug must be administered at one site only at one time. It cannot be allowed to contact so much as a drop of water. Directions are also given for checking for moisture and uniform suspension in bottles which have been stored.

It is well to have some intocostin readily available in the patient's room to be administered intravenously if immediate relaxation is necessary and there is insufficient time for an intramuscular injection of curare in oil to act.

We cannot emphasize too strongly the necessity for the following when curare in oil and wax is used in the treatment of tetanus:

1. Constant nurse attendance
2. Presence of the following at bedside:
 - a. Tank of oxygen with mask, canister and breathing bag so that artificial respiration with 100 per cent oxygen can be given immediately
 - b. Catheter suction
 - c. Laryngoscope and endotracheal tubes
 - d. Tracheotomy tray

3. Availability of Drinker Respirator

Finally, the treatment of tetanus with curare is not without danger, but if curare in its present improved form can do anything to lessen the high mortality of this disease, it would seem to be worth all the effort that use of the drug necessitates.

SUMMARY

Two cases are reported of tetanus successfully treated with d-tubocurarine chloride in peanut oil with myricin. It is brought out that the chief advantage curare has over the hypnotic drugs is that it relaxes as they do but does not do so at the expense of consciousness. The curare preparation is not so short-acting and difficult to control as previous curare preparations have been. Precautions necessary in the use of this drug are emphasized.

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