

Recent Discoveries in the Treatment of Lockjaw with Vitamin C and Tolserol

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SECOND IN A SERIES OF TWO

The purpose of this paper is to dispel the popular belief that tetanus is a difficult disease to cure. It is bold, but correct to say that the number of cases terminating fatally from the disease are equaled by those who die from the treatment. Evidence will be presented to show that the antitoxin has no curative value and at the best is harmful. Convulsive seizures must be controlled, but it is wrong to employ a drug for this purpose that tends to deprive the patient of his sensorium. Many patients have been lost, not only with tetanus but also from the many other disease conditions, simply because the treating physician blindly followed a recommendation set down by a colleague who by "Fate" was in a position of authority. Too few of those who write appreciate the responsibility of their words. Unfortunately, in medicine, the driver's seat is still at the back. It is rare, indeed, to find any two authorities offering the identical treatment for any given disease. Some much used volumes give five, ten, or even fifteen different remedies for a given disease; this can only lead to "coin tossing." Yet MAN in his search for health still comes to the doctor. This condition will prevail until we assume enough courage to have but ONE textbook for the practice of medicine; this should be loose-leaf.

Case History: White boy of 6 years. Did not receive the required pre-school injections. Severe asthmatic since infancy. Reported to have had diphtheria March 1951; no smears or culture made. Present illness thought to have started three weeks before admission with severe attack of asthma which lasted for two weeks. This episode was associated with abdominal cramps, unexplained at the time, and a generalized sensation of muscle tightness. Six days before admission he developed drooping of the eyelids. He also found it difficult to smile (perpetual with this boy under normal circumstances) and there was definite resistance whenever he attempted to fully open his mouth, like in a yawn.

Abdominal cramps were now more pronounced and they were experienced more frequently. Two days prior to admission his abdominal muscles assumed boardlike rigidity which was synchronized with the abdominal pain and these episodes were being experienced more often while increasing in duration. His diet was self limited to liquids due to the inability to open his mouth more than 30%; this created pain at the temporomaxillary joint and was always followed by the sudden "involuntary" clamping of his jaws. On the day of admission he had progressed to a stage when the slightest stimulation would contract his back muscles with such force that he would form an arch with his body resting on his feet and head. Sweating was profuse during this time; respirations were absent. When the clonic spasm was released he would lie limp and exhausted.

The physical examination added little to this picture. The temperature was 100.4° F., respirations shallow 20 to 25 per minute, the pulse was rapid but not thready, running between 120 and 130. He could "push" his tongue to the margin of his lips and a facial expression was impossible. A few "terminal rales" could be heard in both lung fields. The right patellar reflex was exaggerated and since this elicited a convulsive seizure the other reflexes were not attempted. His course in the hospital was interesting but not dramatic. The most trying period was spent in combating the pathology resulting from allergy. There was a history of a fall in the pony yard resulting in "brush burns" of his hands about one week before the onset of the "peculiar asthma attack." (It must be added that many a devout person offered sincere prayer for this lad's recovery. I humbly submit that Providence in hearing these supplications, did employ my intellect in carrying out His design.)

In the past it was thought that successful therapy depended upon four factors: (1) Early and adequate use of antitoxin; (2) Sedation to

the point of narcosis; (3) Wound débridement; (4) Competent, intelligent, continuous nursing; (5) Five percent hydrogen peroxide to which Tr. of iodine has been added for cleansing the wound, magnesium sulfate given intravenously as a 20% solution in the amount of 50 cc, curare, frequent warm baths, spinal tap with replacement of fluid with anti-tetanus serum and a quiet, dark room.

Today the treatment of tetanus has resolved itself into a plan best suited to combat the convulsive seizures. Except for one single dose of antitoxin (75,000 units) given deep intramuscularly above the portal of entry if this is known or is possible, the use of this "agent" should be forgotten. Its employment, presently, is intended more for the legal protection of the attending physician rather than for the betterment of the patient. Our case will prove that it has no value and in all probability was harmful. Teale and Embleton reported that the toxin does not pass from the capillaries to the tissue of the central nervous system, nor from the choroid plexus to the cerebrospinal fluid, and that it is blocked from reaching the cord along the afferent nerves by the posterior root ganglia. By inference they concurred with Meyer and Ransom in believing that the path taken by the poison was the motor nerves. MacCallum pointed out that the antitoxin cannot travel from the circulation into the nervous system and that unless it be injected into the nervous tissue, it is relatively valueless. Meyer and Ransom showed that the injection of antitoxin into the nerve ABOVE the point of inoculation would BLOCK and neutralize the toxin. Davison advocates the use of tetanus toxoid 0.1 cc given intradermally for five consecutive days as a means of boosting the patient's antitoxin titer.

The most important therapeutic measures available are massive doses of vitamin C and Tolserol, both given intravenously. Jungeblut reported that vitamin C, when added to tetanus toxin "in vitro," brings about inactivation of the toxin. He felt, however, that the mechanism of the inactivation of tetanus toxin by vitamin C was fundamentally different from that of toxin-antitoxin reactions. In one experiment he observed that guinea pigs injected with a mixture containing critical amounts of toxin and vitamin C died with tetanus if the mixture was not in-

cubated and LIVED if the mixture was previously incubated. (We believe the human body to be a first class incubator.) This work of Jungeblut followed, in a fashion, the findings of Imamura who, in 1929, reported inactivation of tetanus toxin by adding it to ovarian follicular fluid. Corpus luteum is now known to contain a high concentration of vitamin C. We have found massive doses of vitamin C to be dramatically effective in hundreds of cases in which the offending poison was an exotoxin or a virus. (Here I must inject the story of a four-year-old child bitten on the leg by a mature, highland mocassin. This case is related to tetanus in that both conditions offer the "exotoxin" as the killing agent. The child was bitten at 7 p.m. while playing in the yard. Seen in the emergency room of the local hospital at 7:30 p.m., she was vomiting, was crying because of severe pain in her leg which she held above the "fang marks" and had a 99.2° F. fever. Four grams of vitamin C was given intravenously at 7:35 p.m. The following 35 minutes was taken up preparing and skin testing anti-venom serum which was given at 8:00 p.m. At this time and before the anti-venom was administered she had stopped vomiting, had stopped crying and was sitting on the emergency room table laughing while she drank an orangeade. Her comment was: "Come on, daddy, I'm all right now." She was not admitted to the hospital but was allowed to return home with the understanding that the father would give me a report, by telephone, each hour throughout the night. This he did. His report each time was that she was sleeping as she usually did, and that other than a small amount of swelling up to the calf of her leg, appeared normal. She was seen in my office the following morning at 10 a.m. At this time she had ½ degree of fever and about the same amount of swelling described by her father during the night reports. She had had a "big" breakfast and wanted to know if she could play when she retruned home. She was given 4 grams of vitamin C intravenously and sent home. Seen the same day at 5:00 p.m. she had no fever and about the same amount of swelling. She was given 4 grams of vitamin C intravenously. The following morning, 38 hours after being bitten, she was completely normal. As a precautionary measure 4 grams of vitamin C was given intra-

venously. This was the end of the snake bite, except that she carried the fang marks for a considerable time. No other antibiotic was given for secondary wound invaders as a result of the bite and none was required. This treatment was first worked out by me in dogs and published in hunting and fishing magazines. Several physicians have cured rattlesnake bites using this treatment schedule; their voluntary letters are in my files.) The vitamin must be given by needle in massive doses and around the clock to obtain these results.

Intravenous TOLSEROL, given in adequate amounts, has no equal in controlling the convulsive seizures found in tetanus. In our case of the six-year-old boy weighing 20 Kg. we gave as an initial dose 200 mg of Tolserol in 500 cc of D5 water at a rate of 35 drops per minute. Since no dose schedule was available for children at that time (September 1951), we experimented with this amount since we did not desire too great a relaxation. Prostigmin was made available for this emergency. There was no response to this amount of Tolserol, so after six hours an additional 800 mgm was given, using the same type of diluent. The results obtained proved that this was the drug of choice in producing relaxation and preventing convulsive seizures in tetanus. This fact was apparent before the fluid run was completed. Subsequent doses of Tolserol were set at 1000 mgm. This amount gave complete control of all muscle spasm for a period of 60 hours. Under the influence of intravenous Tolserol the patient immediately began to take nourishment by mouth, was not disturbed by noises in excess of what should be expected in a hospital and did not require a darkened room. Nursing care was limited to that given by "floor nurses," although we did keep a companion in the room at all times as a psychological measure. The same day that intravenous Tolserol was given the patient played with toys in his bed and used crayons to color pictures in a color book. After about 60 hours this interest was suddenly lost and mild spasms returned. This pattern was just as suddenly reversed by giving another 1000 mgm of Tolserol intravenously. Other types of therapy were employed in this case. A review of his hospital course will argue the case for vitamin C and intravenous Tolserol. At only one period

of his hospitalization was the outcome in doubt and this was due to a reaction to serum. Here again Tolserol and vitamin C saved the day.

He was admitted 9/1/51 at 30 minutes past noon. Two grams Vitamin C were given intravenously at 1:00 p.m. Liquids taken freely throughout afternoon. 6:00 p.m. 2 grams of vitamin C. (All vitamin C and Tolserol given in this case was administered intravenously.) At 8:15 p.m. child reported crying loudly. A.S.A. grains V given by mouth with some difficulty. 9:00 p.m. 2 grams of vitamin C. At 10:40 p.m. an S.S. enema was given with good results. The procedure did not excite muscle spasm. 12:00 midnight 4 grams of vitamin C and one 10 cc ampule calcium gluconate. Child sleeping. At 3:00 a.m. 4 grams vitamin C. Patient having moderate abdominal cramps; no difficulty in swallowing. 6:00 a.m. condition same; given 4 grams vitamin C. 8:00 a.m. some difficulty in swallowing; 4 grams vitamin C given at 9:00 a.m. and by 10:00 a.m. was resting quietly. Sleeping at 11:00 a.m. and at 12:00 noon voided 100 cc urine. (From this point kidney output was normal.) Taking fluids freely by mouth. At 1:00 p.m. 4 grams vitamin C and 600,000 units procaine penicillin. The entire afternoon was spent "lying quietly" in bed. Fluids now protinal in milk and egg in milk; no difficulty in swallowing. At 6:00 p.m. and 9:00 p.m. 4 grams of vitamin C. Nembutal suppository grains 2 ordered by intern but there was no restlessness. The explanation for this order was "so the boy would get off early to sleep." At 12:00 midnight was given aspirin grains V, 4 grams of vitamin C and 600,000 units procaine penicillin. The rationale of the penicillin was to prevent secondary pulmonary pathology. The night of September 3rd was uneventful; he received 4 grams of vitamin C at 3:00 a.m. and at 6:00 a.m. Had mild abdominal cramps, off and on, through the morning. At 10:00 a.m. 4 grams of Vitamin C; sleeping at intervals. Because of "outside pressure" 25,000 units TAT were given with saline intravenously, after skin testing for sensitivity. This was at 12 noon. By 1:00 p.m. his temperature was up to 101° F. rectally, the highest since admission; refused egg in milk. 2:00 p.m. voided 300 cc urine. At 3:00 p.m. he was crying because of severe pain in his abdomen. Floor nurse reported in her daily log—"an uncom-

fortable period since antitoxin." 4:00 p.m. 4 grams vitamin C, refused all liquids but by 5:00 p.m. was sleeping. Since antitoxin therapy was not our decision we elected to be heroic and give it a test to prove its lack of value.

(I will never forget a case of "lockjaw" in an adult white female that was my duty to treat as a house physician at Moore County General Hospital in 1937. Notes which I made at that time show that this patient died from asphyxia less than one hour after receiving 30,000 units of tetanus antitoxin intravenously. The serum was not diluted in saline as we employed in this case but it was given very slowly. Intravenous sodium amytal failed to release the convulsive seizure in this woman.)

At 8:00 p.m. 50,000 units T.A.T. in saline given intravenously; 4 grams of vitamin C given after completion of antitoxin. 9:00 p.m. he was, as before when T.A.T. was given, crying because of severe abdominal pain; his back was rigid and bowed. This picture continued fairly constant until 12:00 midnight; 4 grams vitamin C and 600,000 units penicillin given. By 1:00 a.m. he was resting comfortably and by 2:00 a.m. the nurse recorded—"abdomen more relaxed, still has slight attacks of pain but much further apart." 4:00 a.m. 4 grams vitamin C and he slept until bath at 7:00 a.m. At 8:00 a.m. 50,000 units T.A.T. intravenously in saline; aspirin grains V. 9:00 a.m. was having frequent sharp abdominal pain; nourishment by mouth was a bottle of carbonated drink and $\frac{1}{2}$ glass of milk. 12:00 noon 4 grams vitamin C and 4 grams again at 4:00 p.m. Comfortable throughout afternoon. At 7:30 p.m. 20,000 units tetanus antitoxin and crying out because of severe abdominal pain by 9:00 p.m.; refused all fluids by mouth. At 11:30 p.m. 500 cc 10% glucose in saline containing 4 grams vitamin C. September 5th. Attacks of muscle spasm more severe than at any other time. 12:00 midnight, 600,000 units procaine penicillin and 4 grams vitamin C; same amount of the vitamin at 4:00 a.m. and 8:00 a.m. Fairly normal sleep from 3:00 a.m. to 7:00 a.m. At 9:00 a.m. 300,000 units T.A.T. in saline intravenously; severe convulsive-like seizures of abdominal and back muscles reported at 11:00 a.m. 12:00 noon 4 grams vitamin C; sleeping quietly by 1:00 p.m. Oil retention enema given at 2:00 p.m. but unable to retain. Because of very severe seizures

in which patient's body arched off the bed which was accompanied by profuse sweating we decided that if our little patient was to live some NEW type therapy must be adopted. Accordingly, 200 mgm of Tolserol in 500 cc D5 in water was started, the flow being 35 drops per minute. (This was an experimental dose since we could find no reports on the use of Tolserol intravenously in children.) 8:00 p.m. 4 grams vitamin C and 30,000 units tetanus antitoxin in saline at 9:00 p.m. Crying because of severe abdominal pain at 10:30 p.m.; also very restless and absolutely unable to swallow. September 6th. 12:00 midnight, 4 grams vitamin C and 600,000 units procaine penicillin. No response was observed after 6 hours with the 200 mgm. of Tolserol, so we elected to give 800 mgm. Tolserol in 500 cc D5 in water at this time, employ the 35 drops per minute schedule. 1:00 a.m. patient was resting quietly; asleep at 1:30 a.m. This continued until bath at 7:00 a.m. except for an occasional interruption caused by asking the patient how he felt. This was done to evaluate the degree of relaxation present; each time he responded gently that he was "feeling fine" and then returned to his slumbers. Vitamin C now given at 12-hour intervals maintaining the same dose schedule. 12:45 p.m. 20,000 units T.A.T. in 5% glucose in water and at 9:00 p.m. 28,000 units tetanus antitoxin in saline, both intravenously. It was of great significance to note that this time there were no exacerbations of muscle spasms—the Tolserol was doing a good job. September 7th was relatively uneventful. Three cc aqueous solution adrenal cortex was given every 8 hours for three times to relieve the strain on this gland. 5:00 p.m., we really began to hear from our tetanus antitoxin as the first urticarial wheel appeared on patient's right forearm. Benadryl 10 mg. and Kutapressin $\frac{1}{2}$ cc were given intramuscularly; one hour later 20 mgm benadryl and 3 mm adrenalin. Calamine lotion with phenol to whelps which by 9:00 p.m. had covered the entire body. Adrenalin 3 mm and benadryl 10 mg were given every 30 to 60 minutes, alternating, until 2:00 a.m. following day. Calcium gluconate 10 cc given intravenously. In spite of this therapy the stimulation from this serum reaction was enough to re-excite the muscles into painful spasms. At 11:30 p.m. 1000 mgm Tolserol in 500 cc 5%

glucose in water was started. It was a rough night. By 3:00 a.m. the Tolserol was taking hold and "all was well" by 6:00 in the morning. Following this episode streptomycin was substituted for the penicillin in the light that it, too, might have played a part in the allergy. From this time until discharge kutapressin, benadryl, and B-Complex were employed freely. Intradermal tetanus toxoid was given daily the last five days in the hospital. From this day on nourishment was taken freely when offered and muscle pain and spasm was absent. He was discharged on the 18th hospital day but could have safely returned home 10 days before. This we did not know at the time.

Vitamin C was employed for the following reasons: (1) Its antihistamine like action; (2) For its diuretic effect; (3) For its ability to neutralize exotoxins; (4) For its role in antibody formation. It is interesting to note that on September 8th, 10 days before discharge, the white blood count was 4,800 and the differential showed 45% lymphocytes and 55% polymorphs. Kracke states that one of the most notable instances of the increase of lymphocytes above normal is in recovery from acute infections. Kracke reports that Wintrobe gives as a fact: "That the lymphocytes are active in antibody formation."

In summary the following schedule will serve well in the treatment of TETANUS: (1) A debridement if a "ragged" wound is present; (2) Clean the field well. Any good antiseptic, applied thoroughly, will serve to sterilize the field. (Ether is too seldom used. It will destroy most bacteria, even colon bacillus, without injuring protoplasm.) Sterilizing of the wound when present, is done, not so much against the bacillus tetani which is highly resistant but for the destruction of other pathogenic or even non-pathogenic organisms. Park and Williams report that it has been found that pure cultures of tetanus, after the germs have sporulated and the toxins been destroyed by heat, can be injected into animals without producing tetanus.

But if pathogenic streptococci or staphylococci or even non-pathogenic organisms are injected simultaneously with the spores, or if there is an effusion of blood at the point of injection, or if there was a previous or later bruising of the tissues, the animals surely die of tetanus. The spores under such conditions can develop and produce the disease. For this reason one should give 75,000 units antitoxin deep intramuscularly above the wound when present and when possible. (3) Intravenous fluids; (4) intradermal tetanus toxoid 0.1 cc for five consecutive days; (5) Massive doses of vitamin C around the clock and given by needle; (6) intravenous Tolserol in adequate amounts. In our case 1000 mgm for a body weight of 20 Kg. was adequate. One can only hope that all the states will adopt legislation requiring annual booster injections of tetanus toxoid for all people regardless of age. This to be given at the expense of the states with the co-operation of its practicing physicians.

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