

THE MANAGEMENT OF SEVERE SYSTEMIC TETANUS *

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Received for publication March 5, 1952

OFTEN the therapeutic measures utilized in controlling disease conditions and symptoms are devoid of sound physiologic principles. This is the case in the management of the severe tetanic episodes of systemic tetanus. In the past, the high mortality rate, in part, was indicative of our inability to control, therapeutically, the violent spasms. Patients died from hypoxia or exhaustion, or both. The hypoxia was the result not only of an unmanageable airway but of tonicoclonic contractions of all the respiratory muscles, including the diaphragm.

Current advances in symptomatic therapy are representative of a more physiologic approach; for example, the advocacy of early routine tracheotomy (1) and the intramuscular use of one of the curariform drugs to minimize the severity of the tetanic spasms (2). In contrast to the logic of these two steps, the traditional use of massive doses of depressant drugs still persists. Despite all of the above measures (tracheotomy, curare and depressants), the severity of the contractions frequently becomes so great that their control results in deep central narcosis and muscular paralysis which leads to fatal respiratory depression.

Recent developments in the management of patients who have total respiratory paralysis associated with poliomyelitis suggested a logical solution to this problem. Briefly, the core of symptomatic therapy for severe tetanic spasms involves the production of a flaccid paralysis and the maintenance of artificial respiration. Under these conditions the general physiologic state can be sufficiently regulated so that the time required for effective specific antitoxin and antibiotic therapy is attained.

The purpose of this article is to emphasize the exigency for controlling the tetanic phases of systemic tetanus without the use of central depressants and to outline methods whereby normal respiratory physiologic functions can be maintained. The details of antitoxin and antibiotic therapy will not be discussed.

Effective symptomatic therapy should encompass primarily two physiologic principles: (1) the establishment of a normal respiratory exchange and (2) the prevention of an increased oxygen barrier at the cells.

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Respiratory Exchange.—The spasms associated with severe systemic tetanus defeat most attempts to maintain a patent airway and adequate ventilatory exchange. Certainly, patients who manifest hyper-irritability, trismus, minor clonic contractions and bouts of cyanosis require immediate tracheotomy. (At this institution, tracheotomy is a routine procedure after the diagnosis has been established.) Tracheotomy is a simple procedure under ordinary circumstances but in the presence of tetanus, it is complicated by the tetanic response of the patient to slight stimuli. For this reason, regional and most general types of anesthesia are contraindicated. The anesthetic of choice should be moderately soporific, powerfully relaxant and permit the use of high oxygen tensions. An ultra-short acting barbiturate in conjunction with flaxedil®† is ideal. Administered intravenously, it provides rapid induction, complete muscular relaxation and permits the use of high oxygen tensions. In effect, this combination completely eliminates muscular spasm, permitting an adequate airway and artificial respiration to be maintained.

As soon as practical, after completion of the tracheotomy, the patient is placed in a Drinker-Collins respirator and a tracheotomy inhalator (3) is attached by means of a "T" type inner cannula. The inhalator is equipped to deliver a helium-oxygen mixture, thereby avoiding "oxygen poisoning" and maintaining alveolar inflation. The entire respirator should be in Trendelenburg position to facilitate postural drainage of the tracheobronchial tree. The general supportive therapy and constant supervision required by patients in respirators (4) who have poliomyelitis, also applies to the curarized patients who have tetanus. These patients must have their positions changed frequently; the tracheobronchial tree must be aspirated often; daily chest roentgenograms are of first importance in detecting the development of atelectasis and pneumonia; a bronchoscopy should be done when catheter aspirations fail to remove mucous plugs from the bronchial tree, and antibiotics are used freely for prophylaxis and therapy of pulmonary infections. To facilitate good nursing care, the patient should be removed from the respirator daily.

During severe tetanic seizures muscular rigidity develops which inhibits adequate ventilation of the lungs, in spite of the respirator. It is imperative that muscular spasm be released effectively so that normal respiratory exchange may be maintained by artificial means. Skeletal muscular flaccidity is obtained rapidly by the *intravenous* use of one of the myoneural blocking agents.

Of historical interest is the fact that curare and curarine alkaloids were used in the control of systemic tetanus as early as 1867 (5). In 1935, Cole (6) recommended curare as a last resort for patients who would certainly die unless some additional therapy was instituted.

† Flaxedil (supplied by courtesy of Lederle Laboratories Division, American Cyanamid Company, Perl River, New York) is the tri-iodo salt of tris (triethylaminoethoxy) 1, 2, 3 benzene, a synthetic curariform drug.

Curare was used by Isacson and Swenson (7) in 1940 to control tetanic spasms for the first time in this country. In 1943, Cullen (8) described a course of treatment utilizing curare for the control of tetanic episodes. Subsequently, preparations of curare in oil and wax were developed for intramuscular use. These preparations are satisfactory in the treatment of mild systemic tetanus but cannot be relied upon in the severe cases which require continuous muscular flaccidity.

By means of intravenous administration, curariform drugs produce rapid relief of muscular spasm and the regulation of the dose can be adjusted easily so that no more than the minimal effective requirement is utilized. The individual dosage increments and the frequency of administration are determined by trial and must be sufficient to prevent tetanic muscular responses to stimuli at all times. With curarization, all necessary technical procedures involved in nursing care may be accomplished without the precipitation of muscular spasms. Analgesic drugs should be markedly curtailed since the severe pain associated with tetanic spasm is abolished with the onset of relaxation.

The choice of the myoneural blocking agent deserves careful consideration. Several of the drugs have undesirable side effects which should be avoided in prolonged and continuous administration. At present, flaxedil (9) possesses the most desirable advantages. The onset and peak of actions are attained most rapidly with this drug. It does not produce blockage of the autonomic ganglia as do *d*-tubocurarine and dimethyl curare. It is selectively depressant to the cardiac vagal fibers. An increase in the heart rate and a slight elevation in the blood pressure are clinical effects which are unique to flaxedil. The histamine-like action of the naturally occurring curariform drugs is not discernible with the use of flaxedil. Unlike syncurine®, ‡ flaxedil is readily antagonized by tensilon® § and prostigmin®.

Prevention of Increased Oxygen Barrier at Cells.—Provision for an adequate airway and minute volume exchange of gases in the totally relaxed patient accomplishes delivery of oxygen to and removal of carbon dioxide from the blood stream but does not assure proper tissue respiration.

Cellular oxidation, particularly of the central nervous system, is of major import. The patient who has tetanus suffers not only cerebral cellular hypoxia because of anoxemia, but also, actual cellular damage which results from the action of the tetanus toxin itself (10, 11). For these reasons, massive doses of central depressant drugs should be avoided. Paraldehyde, avertin, chloral hydrate, opiates, bromides and barbiturates are all central depressants when utilized in doses large enough to control severe convulsions. In addition, the mode of action of these drugs is presumed by many to be the result of interference with the cellular oxidative mechanisms. Quastel and Wheatley (12) have demonstrated that soporific agents inhibit the oxidative reactions *in vitro*

‡ Syncurine, Burroughs Wellcome and Company, Inc., brand Decamethonium bromide.

§ Tensilon, Hoffman-LaRoche, Inc., brand 3-hydroxy phenyldimethylammonium bromide.

of brain slices. It has been shown that the cerebral arteriovenous oxygen difference is reduced during anesthesia, indicating a lowered oxygen consumption by the brain (13, 14, 15). Certainly, the use of depressant drugs, for the control of tetanic spasms, is unphysiologic if their mechanism of action is by oxidative interference with cerebral cells which already suffer from severe hypoxia. Soporific drugs in patients with tetanus are indicated for the production of normal sleep and the allaying of apprehension. The doses should remain within the normal range of usage for this purpose.

CASE HISTORY

C. L., a 5 year old white girl, was admitted to the University Hospitals at 3:00 p.m. on September 29, 1951, because of intermittent episodes of trismus, stiff neck and generalized clonic spasms accompanied by dyspnea and dysphagia. One week before these symptoms began, the child had sustained a deep wound of the buttocks which involved the gluteal muscles. On admission, this wound was partially healed but was indurated and red.

The diagnosis of tetanus was made and sodium phenobarbital, 2 grains, was immediately given intravenously. By 8:00 p.m., the increasing gravity of the situation was recognized and tracheotomy was performed under pentothal-curare anesthesia. In addition, extensive debridement of the gluteal wound was carried out and a polyethylene tube was placed in the saphenous vein for intravenous therapy. The entire surgical procedure required about ninety minutes, during which time the patient was well relaxed, her color was excellent and vital signs were stable. She was returned to her bed at 9:30 p.m. without evidence of muscular spasm and remained so until 12:30 a.m. on September 30, 1951, when minor clonic responses to stimulation again appeared. By 1:30 a.m., sedation was given to control the seizures. The patient's condition became progressively worse, in spite of large doses of paraldehyde rectally and sodium luminal intravenously. By 11:00 a.m. on October 1, 1951, the tetanic episodes had become so severe that they appeared to be continuous. The child was in extreme opisthotonos and was deeply cyanotic although she was in an oxygen tent, the pulse was rapid and feeble, and the rectal temperature had risen to 106 F. The patient obviously was moribund.

At 11:07 a.m., 90 mg. of flaxedil was administered intravenously; within one and a half minutes, complete relaxation occurred. An endotracheal tube was introduced through the outer cannula of the tracheotomy tube and artificial respiration with 100 per cent oxygen was instituted by means of an anesthesia machine. Cyanosis immediately disappeared and the pulse became stronger. When the patient was considered to be sufficiently oxygenated, extensive tracheo-bronchial aspiration was carried out without interruption of oxygen delivery to the child. This was effective in removing many large mucous plugs. However, a portable roentgenogram of the chest, taken immediately after this procedure, revealed atelectasis of the upper lobe of the right lung. Bronchoscopy was then carried out with the removal of additional plugs but the lobe did not improve radiographically. A Wangenstein gastric tube was inserted to prevent the regurgitation of stomach contents. The high body temperature was reduced rapidly with alcohol sponges and enemas of ice water; it was 102 F. at 2:15 p.m. The patient was then placed in a Drinker-Collins respirator and a circle type of

oxygenator was adapted to the tracheotomy tube. *All sedative drugs were discontinued.*

During the remainder of October 1, 1951 and the early part of October 2, 1951, the patient did quite well, and required about 10 mg. per hour of flaxedil to control the tetanic movements. Her color was well maintained and the vital signs were stable. She remained unconscious, probably as the result of both the severe hypoxia and the massive sedation which existed prior to curarization.

The temperature was 102 F. until 5:00 p.m. on October 2, 1951, at which time it rose to 105.4 F. During the next eight hours, the patient apparently reached the peak of her illness: the severity of the convulsive movements increased, and 60 mg. of flaxedil per hour was required for adequate control. Large quantities of tracheal secretions were released and brief bouts of cyanosis occurred if the curarization was allowed to lighten. The output of urine was very scant; the temperature remained high and the pulse became rapid and weak. By the early morning hours of October 3, 1951, her condition appeared to improve, and only about 20 mg. of flaxedil per hour was required for control of the tetanic seizures. The temperature fell to 102 F. and vital signs improved. She still did not respond. Therapy was continued, with emphasis on frequent changes of position and constant attention to the tracheal secretions. On the morning of October 4, 1951 (three days after loss of consciousness), she showed the first sign of response by grimacing whenever the trachea was suctioned. Flaxedil, 10 to 20 mg per hour, was still necessary to avoid tetanic movements. Heavy mucus in the tracheobronchial tree with formation of plugs continued to be a problem and on the afternoon of October 4, 1951, another bronchoscopy was necessary. The atelectasis of the right upper lobe was not improved despite antibiotic therapy.

On October 5, 1951, there was evidence of continued improvement. The patient was awake and responded to her name. Tetanic muscular spasms were less frequent and severe, and only about half the previous dosage of flaxedil was required. Tracheal secretions were less profuse and the lungs were well aerated with the exception of the involved lobe. By October 6, 1951, administration of flaxedil could be stopped completely, and soon adequate respiratory exchange could be maintained without the aid of the respirator. The patient was alert to her surroundings and her condition had become stabilized in all respects. A portable roentgenogram of the chest revealed that atelectasis of the left lower lobe of the lung had developed. There was only slight improvement in the appearance of the right upper lobe.

By October 11, 1951, the pneumonic process of the left lower lobe had become resolved and by October 15, 1951 the right upper lobe showed only slight residual changes.

The patient's condition improved steadily from that point, the tracheotomy stoma was allowed to close and she was discharged on October 24, 1951. At examination, one month later, no obvious sequelae were revealed.

SUMMARY AND CONCLUSIONS

The lethal respiratory abnormalities that accompany severe systemic tetanus are presented.

More radical methods for securing and maintaining complete control of respiratory ventilation are advocated and the physiologic justification for adoption of such methods is explained.

Curtailment of massive doses of central depressants is stressed.

A case history demonstrating complete salvage of a moribund patient with tetanus is presented. It is of interest to note that six days of continuous curarization was required.

It should again be emphasized that the measures suggested constitute a radical form of treatment intended for the severe convulsive phases of tetanus. Such treatment necessitates personnel experienced in the handling of respiratory emergencies, the use of curariform drugs and the operation of respirators.

It is suggested that such a regimen may be useful in the control of other acute convulsive disorders that impair respiration. By this means, adequate time would be provided for establishment of the diagnosis and institution of specific therapy.

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