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THE CLINICAL, BACTERIOLOGICAL, AND METABOLIC ASPECTS OF A CASE OF TRAUMATIC TETANUS; TREATMENT WITH TETANUS ANTITOXIN; RECOVERY.¹

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I. CLINICAL COURSE AND TREATMENT.

BY HENRY HEIMAN, M.D.

INASMUCH as the reported cases of true traumatic tetanus treated with subcutaneous and intraspinal injections of antitetanic serum

¹ Read before the Harlem Medical Association, N. Y., May 3, 1905.

are not numerous, we feel justified in placing on record the facts of the following case:

The patient, a boy twelve years of age, was admitted to Mount Sinai Hospital on the night of August 11, 1904. Two weeks previously he had stepped on a nail, which perforated the sole of the shoe and penetrated the ball of the right foot. A physician who was summoned incised the wound, which, ten days later, was entirely healed. There were no constitutional symptoms till eleven days after the accident, or three days before admission. Early on the morning of that day, without warning, the boy fell to the floor in his home. There were no convulsions or unconsciousness. Saliva dribbled from the mouth and the boy complained of pain in the back. After that he was apparently sick; he complained of severe backache, loss of appetite, and on the morning of the day of admission he was unable to open his mouth. He was still able, however, to swallow fluids. At about 11 A.M. there were noticed a staring countenance, rigidity of the neck, back, and legs, and hyperacusis. There were noticed, also, twitching of the muscles of the face, trunk, and extremities. There were, according to the family, no headache, unconsciousness, fever, chills, or involuntary urination. The bowels had not moved in three days. Perspiration was very profuse. The chief complaints were inability to open the mouth and pain in the back.

On admission a *physical examination* by Dr. Bauman, the house physician, showed the following: General condition fair. There are present trismus, risus sardonicus, opisthotonos, rigidity of the neck, and contraction of the muscles of the abdomen and back. No facial or ocular palsy. The pupils are equally contracted. The throat could not be inspected. No difficulty in swallowing fluids. Slight enlargement of the lymph nodes in the neck, axillæ, and groins. Kernig's sign is present. The Babinski reflex is present. The patellar reflexes are exaggerated; heart and lungs negative; liver palpable two fingers below the free costal border; spleen negative; abdomen somewhat rigid; temperature, 99°; pulse, 104 in frequency, of good quality; respirations, 18; they are irregular, and at times there is stridulous inspiration. The urine shows a trace of albumin, otherwise negative. On the sole of the right foot, in the region of the distal extremity of the first metatarsal bone, is a small scab about the size of a lentil. The house physician immediately removed the scab; under aseptic precautions he incised and curetted the wound, and then cauterized it with silver nitrate. In the scrapings was a small, black, foreign body resembling leather in appearance; this, together with the curetted tissue, was sent to the pathological laboratory of the hospital, a report from which is included in this paper.

On August 11th, the night of admission, there was given in the right pectoral region a subcutaneous injection of 20 c.c. of Board of

Health tetanus antitoxin. An hour later a lumbar puncture was performed and 5 c.c. of cerebrospinal fluid were withdrawn. This was followed by a subdural injection of 20 c.c. of tetanus antitoxin. During these procedures the slightest sound or touch would cause the boy to start. In attempting to swallow some fluid nourishment, the muscles of his entire body suddenly became contracted. Twelve hours after the first subcutaneous injection another one was given. The wound was dressed and touched with a 10 per cent. solution of nitrate of silver.

August 13th. Under chloroform narcosis, after withdrawing 25 c.c. of cerebrospinal fluid, 20 c.c. of tetanus antitoxin were injected subdurally. Six hours later 20 c.c. of tetanus antitoxin were injected subcutaneously into the thigh. A leukocyte count made on this day was 12,600.

14th. During the three days of observation there has been little change in the general condition. The mental condition has been clear. Fever but slight. The spastic signs persist; there are still present trismus, risus sardonicus, opisthotonos, and hyperacusis. While attempts to raise the patient's head are followed by contraction of the muscles of the neck and back, lateral rotation of the head can be performed with ease. The patient swallows and retains sufficient fluid nourishment. The medication has been chloral and bromides, at first per rectum, later by mouth, and whiskey per mouth. The intraspinal and subcutaneous injections of antitoxin were given to-day as previously.

16th. Subcutaneous injection repeated. Catheterization was necessary yesterday.

17th, 18th, and 19th. Spastic signs persist. A subcutaneous injection of 20 c.c. of antitoxin given on each day.

20th. The temperature has risen to 102° and an erythematous eruption has appeared on the chest, abdomen, back, and thighs. White blood corpuscles, 13,800. Trismus, rigidity of the neck, and opisthotonos still present. General condition unchanged.

26th. The erythema, fading on the trunk, is now present on the face. No change in the general condition or spastic signs. White blood corpuscles, 10,400.

28th. The general condition is improving, the spasticity is diminishing. The temperature is still between 100° and 102°; rash almost disappeared. Examination of the heart and lungs is negative. The urine, except on the day of admission, has been negative.

September 1st. Continuous improvement in the general condition. White blood corpuscles, 7800. The rash has faded. The temperature is normal.

7th. The general condition is good. The spastic signs have disappeared.

16th. Patient discharged cured. No symptoms remain.

While a study of the clinical features of this case shows that we

are dealing with a true case of traumatic tetanus, it is worthy of note that an attempt to inoculate ordinarily susceptible animals (white mice and guinea-pigs) with the tetanus bacillus found in the scrapings and foreign body from the wound was not successful.

In the course of treatment between August 11th and 19th, there were given three intraspinal injections of 20 c.c. each, and eight subcutaneous injections of 20 c.c. each, the Board of Health antitoxin being used. To attribute the recovery in this case directly and solely to the antitoxin injections would perhaps be going too far. We cannot help asking ourselves the question: Would a patient with equal resisting powers contracting the disease in the same way have recovered without the antitoxin treatment? We can only say that, in view of the almost uniformly fatal termination of the disease, it is not unlikely that the antitoxin treatment probably effected a cure in this case. When we remember the channel through which the tetanus toxins reach the central nervous system, and when we recall the experiments of Wassermann showing that the union between tetanus toxins and their antitoxins is one produced by a chemical affinity, it would appear that both from a therapeutic and prophylactic standpoint the intraspinal injections are preferable to the subcutaneous or cerebral injections, for by the former method the antitoxin comes in direct contact with the toxins of the disease. This case was taken from the ward of Dr. Koplik during my service.

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II. BACTERIOLOGICAL EXAMINATION.

BY LEO BUERGER, M.D.

The material from which cultures were made consisted of a small, dirty, black, foreign body, apparently a piece of leather, the fatty tissue immediately surrounding it, and scrapings from the wall

of the cavity in which the foreign body was situated. The latter was located at the upper end of the channel through which it had been forced by the traumatism, and was embedded in discolored, necrotic, but non-purulent fat and granulation tissue. The tissue in the immediate neighborhood of the apparently healed external wound was not employed, the examination being confined to material obtained from the depth.

In spreads made from the tissue there were a few leukocytes, red blood cells, and Gram-positive diplococci which were regarded as probably being staphylococci. No organisms resembling tetanus bacilli nor any spores could be found.

The method which Kitasato has recommended for the isolation of the tetanus bacillus was used. This depends upon the observation that its spores can resist exposure to high temperatures for considerable periods of time. Three series of cultures were made: one from the foreign body, another from the tissue in its vicinity, and a third from the cerebrospinal fluid evacuated before the first antitoxin injection. The mode of procedure was the same in each instance. At the end of twenty-four hours' incubation the usual methods of isolation showed the presence of staphylococcus albus and bacillus coli communis in the cultures taken from the foreign body, and staphylococcus albus alone in the tissue. The cerebrospinal fluid remained sterile.

All the cultures were then exposed to a temperature of 80° C. over a water-bath for forty minutes on two successive days. This procedure was followed by incubation under strictly anaërobic conditions (in a hydrogen atmosphere) of both the original tubes and subcultures. Thus pure cultures of tetanus bacilli were obtained from the foreign body and from the subcutaneous areolar tissue.

Although the bacillus isolated in this case resembles the typical tetanus bacillus in almost all of its cultural and morphological characteristics, it presents certain slight variations which are deserving of mention. Firstly, it shows a marked tendency to the formation of oval rather than spherical spores. Secondly, there is perhaps more than the usual amount of variability in regard to the Gram procedure. Whereas it stains positive for the most part, even young cultures are apt to show many bacilli which either partly or wholly decolorize.

On culture media it differs little from the ordinary type. It coagulates milk, and its colonies in gelatin and on agar show less tendency to filiform or lace-like outgrowths.

Animal Experimentations. An interesting feature presented by this bacillus is the absence of virulence for the animals ordinarily susceptible. Whereas white mice and guinea-pigs succumb rapidly to subcutaneous inoculation with the tetanus bacillus, I was unable to kill or produce tetanic symptoms in either guinea-pigs or white mice by the injection of cultures of this bacillus. The following

is a brief *résumé* of the experiments on the pathogenicity of the bacillus.

One guinea-pig and one mouse were inoculated directly with some of the material from which the cultures had been made, and another mouse with the cerebrospinal fluid.

Guinea-pig No. 1. The foreign body (piece of leather) was introduced into the abdominal wall through a small incision, and the wound was closed with silk sutures. Result: no symptoms; in three weeks the foreign body was expelled and spontaneous healing took place.

Mouse 1. Three cubic centimetres of sterile normal saline were thoroughly mixed with some of the tissue about the foreign body. The fluid was injected into the right groin. Result: negative.

Mouse 2. Two cubic centimetres of cerebrospinal fluid were injected into the right leg. Result: negative.

From these experiments the inference is clearly to be drawn that the material from which the bacillus was isolated could not have carried with it tetanus bacilli or spores virulent for these animals. All three animals survived and in none of them were any tetanic symptoms discernible.

Another series of experiments for the purpose of ascertaining the virulence of the bacillus in cultures was made. Four guinea-pigs were inoculated in the leg with varying quantities of bouillon cultures, the smallest dose being one loopful of a four-day growth, the largest 2.5 c.c. of a seven-day culture in plain broth. Three white mice were similarly treated, the largest dose being 1 c.c. of a four-day culture. There was no reaction in any of these animals. With a view to determining whether predisposing factors such as the association of other bacteria or local traumatism would aid in the production of tetanus, another series of animals was employed. Neither by the addition of the bacillus coli communis, nor by the introduction of wood splinters impregnated with the spores of the organism, nor by local traumatism, such as fracture of the bones of the leg, will I be able to give any positive results in guinea-pigs or mice. One guinea-pig died of staphylococcus aureus sepsis, and all the others recovered.

In a recent contribution to the study of tetanus, Vincent¹ calls attention to the influence of heat in heightening the susceptibility of animals to infection with tetanus. By carefully raising the temperature of guinea-pigs in the incubator, their power of resistance was so diminished that even very small doses of only slightly virulent strains would rapidly produce tetanic convulsions. In this way he was able to produce a true tetanus septicæmia. A similar experiment with my bacillus gave negative results. A guinea-pig received an injection of 2.5 c.c. of a bouillon culture

¹ Contribution à l'étude du tétanos, etc., Annales de l'Institut de Pasteur, tome xviii.

in the back. It was then exposed to a temperature of 43° C. in an incubator. In four hours its temperature had risen to 43° C., and twenty minutes later had fallen to 42° C. It was then taken out of the incubator and put under observation. Here, again, the result was negative.

A careful consideration of all the above data naturally leads us to the question as to whether we are dealing here with a true tetanus bacillus.¹ Tavel has described an organism which greatly resembles the true tetanus bacillus, but which is non-virulent for animals. He has found it in many cases of intra-abdominal abscess and especially in appendicular affections. He regards it as an important factor in the etiology of appendicitis. Dr. Libman (personal communication) has also met with a similar organism in pure culture in a case of appendicitis. Tavel's pseudotetanus bacillus, however, although possessing oval spores, differs from the strain that I have isolated in the following points: First, its spores will not withstand a temperature of 80° C. Second, it never possesses more than from eight to twelve flagella, whereas the bacillus under consideration has been found with as many as twenty or thirty.

We must conclude, therefore, that we are in possession not of a pseudotetanus, but of a true tetanus bacillus.

The question as to whether this bacillus is to be regarded as one peculiarly pathogenic for man and avirulent for mice and guinea-pigs, or whether it should be looked upon as having lost its virulence either in the body of the patient or in the process of isolation, it is very difficult to answer. Perhaps further studies upon this and related bacteria will throw some light upon these rather vague and unsettled points. At present, with the data at my disposal, it seems most rational to classify the bacillus with the true but atypical tetanus bacilli.

III. A CONTRIBUTION TO THE METABOLISM IN TETANUS.

BY EDWARD A. ARONSON, M.D.

So little has been accomplished in the metabolism in tetanus that I feel compelled to add my investigations observed in a case admitted to the wards of the Mount Sinai Hospital, in the service of Dr. Henry Heiman, during the past summer.

Before stating my results, I wish to mention that the studies were confined only to the urinary excretion—that is, a determination of the solids, both total and inorganic; the total acidity in terms of HCl; the sulphates, both preformed and ethereal; the total nitrogen; ammonia; chlorine; phosphates and uric acid. Only twenty-four-hour collections of urine were employed, and the work extended

¹ Tavel, *Centralblatt f. Bact. u. P.*, Bd. xxiii. p. 538.

over a period of eight days, divided with an interval of five days into two series of four days each.

The methods used were as follows:

Solids: 5 c.c. of unfiltered urine in a platinum vessel were placed in an oven at 100° C. for three and one-half hours and weighed, giving total solids. HNO_3 and H_2SO_4 were added after igniting, then heated and again weighed, giving inorganic solids as sulphates.

Acidity: 10 c.c. of filtered urine titrated with phenolphthalein as an indicator and determined in terms of HCl.

Sulphates: 50 c.c. of filtered urine treated with 10 c.c. of acetic acid, heated, and 25 c.c. of barium chloride added precipitating the sulphates. This was then filtered, ignited and weighed—this gave me the preformed sulphates. To the filtrate 15 c.c. of HCl were added, boiled until decomposition was complete, filtered, and the precipitate again weighed in a platinum crucible—thus giving the ethereal sulphates.

Total nitrogen: 5 c.c. of unfiltered urine were treated by the Kjeldahl method.

Ammonia: 10 c.c. of filtered urine treated by the Schloesing method.

Chlorine: 10 c.c. of filtered urine were placed in a casserole, NaCO_3 and NaNO_3 added, and then evaporated. After igniting and taking up with hot water, HNO_3 is added to acidify, CaCO_3 to neutralize, and after heating on a water-bath is filtered and washed. The filtrate was then titrated with a $\frac{N}{10}$ AgNO_3 solution with K_2CrO_4 as an indicator.

Phosphates: 50 c.c. of filtered urine to which 5 c.c. of a solution of sodium acetate and acetic acid are added are heated and then titrated with a standard solution of uranium acetate.

Uric acid: To 200 c.c. of filtered urine Folin's method was employed.

Perhaps it would not be amiss to mention the constituents of a normal urine for purposes of comparison later on. Different authorities give different figures; hence there are no arbitrary statistics to be compared with my findings.

Folin,¹ in a very recent publication, gives as the result of an approximately complete and careful analysis of 30 "normal urines" the following figures in a general average:

Amount	143.0 c.c.	Total sulphur	3.31 c.c.
Total nitrogen	16.0	Inorganic sulphate	2.92
Urea	13.9	Ethereal sulphates	0.22
Ammonia	0.85	Neutral sulphur	0.17
Kreatinin	0.58	Acidity	6.17
Uric acid	0.3336	Total phosphates	3.87
Undetermined nitrogen	0.6	Chlorine	6.1

¹ American Journal of Physiology, No. 1, vol. xiii.

These figures were obtained while the patient was subjected to the following diet:

Milk	500 c.c.	Sugar	20 gm.
Cream (18-22 % fat)	300 c.c.	Salt	6 gm.
Eggs (white and yolk)	450 gm.	Water up to	2 litres.
Horlick's malted milk	200 gm.	Water to drink	900 c.c.

In looking into the literature of metabolism in tetanus, I found a series of results in five cases, all adults, reported by Vannini,¹ and I will only mention his conclusions:

"1. The patients required considerable quantities of food, which was but poorly absorbed; hence the marked emaciation.

"2. Increase of albumin metabolism, shown by the marked increase of nitrogen excretion in convalescence.

"3. Scant, concentrated, and hyperacid urine.

"4. Urea and ammonia increased, uric acid excretion diminished.

"5. Often a slight albuminuria with casts.

"6. Rare or doubtful glycosuria.

"7. Chlorine diminished, sulphates and phosphates normal."

My case was a child eight years of age, and the table on page 276 is given with the results of the observation.

These studies were made on urine collected after the first twenty-four hours of his stay in the hospital and for the four succeeding days during which his temperature never exceeded 100.6°, but marked tetanic symptoms were present all this time. The second series of investigations were begun five days after the last of the preceding series was ended, and during the latter period the symptoms had materially decreased and the condition improved much.

In all metabolism work, one of the most important factors is the determination of the total nitrogen excretion. In accurate observations it is necessary to calculate the total nitrogen in the feces as well as in the urine, and for two reasons: first, in ordinary diets a certain proportion of vegetable and animal proteid escapes digestion, and this amount must be estimated and deducted from the total nitrogen intake in order to ascertain what nitrogenous material has actually been used up; second, the secretions of the alimentary canal contain a certain amount of nitrogenous material which represents a genuine excretion and should be included in estimations of the total proteid destruction. Practical experience has shown that in man about 29 per cent. of the total nitrogen of the feces has this latter origin.

During the first period the boy was fed on a fluid diet of milk, coffee, cocoa, and water, but during the second he received a much more nitrogenous diet of soup, milk, egg, cocoa, and rice.

It will be seen on close examination that the table shows us marked increase of nitrogen excretion in the later period over the former,

¹ Contributo allo studio del ricambio materiale nel tetano. *Revista critica di clinica medica*, 1903, Nos. 48, 49, 50.

SOLIDS.					SULPHATES.							
Date.	Amount.	Sp. gravity.	Acidity.	Total.	Inorganic.	Preformed.	Ethereal.	Total N.	NH ₃ .	Cl.	P ₂ O ₅ .	Hu.
August 13, 1904	560 c.c.	1023	25.959	4.15 % 23.24	1.22 % 6.832	0.32 % 1.808	0.02 % 0.1202	1.86 % 10.438	0.21 % 1.165	0.61 % 3.443	0.50 % 2.805	0.07 % 0.4116
" 15, "	440 "	1027	35.0108	6.58 % 28.97	1.048 % 4.6112	0.46 % 2.034	0.02 % 0.098	2.43 % 10.6314	0.25 % 1.092	0.54 % 2.374	0.48 % 2.112	0.057 % 0.2508
" 16, "	320 "	1029	12.0304	7.37 % 23.58	0.95 % 3.0528	0.57 % 1.8198	0.26 % 0.0856	2.56 % 8.189	0.23 % 0.729	0.45 % 0.145	0.36 % 1.152	0.094 % 0.3008
" 17, "	640 "	1018	18.9216	4.22 % 27.03	1.114 % 7.1296	0.203 % 1.297	0.018 % 0.1172	1.389 % 8.8833	0.15 % 0.097	0.74 % 4.77	0.18 % 1.152	0.05 % 0.317
" 22, "	600 "	1019	alkaline	2.95 % 17.70	1.71 % 10.26	0.20 % 1.201	0.013 % 0.076	0.52 % 3.108	0.47 % 2.815	0.40 % 2.385	0.34 % 2.01	0.004 % 0.0225
" 23, "	680 "	1021	14.892	4.15 % 23.22	1.78 % 12.104	0.25 % 1.699	0.015 % 0.099	1.09 % 7.4256	0.08 % 0.566	0.50 % 3.428	0.27 % 1.836	0.08 % 0.408
" 24, "	1060 "	1014	11.607	3.06 % 32.92	1.49 % 15.815	0.14 % 1.52	0.01 % 0.1323	0.35 % 8.9634	0.046 % 0.486	0.34 % 3.612	0.185 % 1.961	0.025 % 0.292
" 25, "	1040 "	1011	15.184	2.37 % 24.606	0.986 % 10.254	0.15 % 1.574	0.01 % 0.1106	0.01 % 11.066	0.056 % 0.587	0.30 % 3.14	0.20 % 2.10	0.007 % 0.0707

despite the fact of an increase of nitrogenous foodstuffs, signifying that the boy was already convalescing and a probable restoration of the "nitrogen equilibrium."

The solids were diminished throughout; sulphates but slightly diminished except on the second day, when the patient received some "salts" for catharsis; ammonia varied, at times increased or normal; chlorine diminished; phosphates but little changed; uric acid much diminished.

The urine was at first scant, concentrated, and hyperacid; later, more copious and less acid. A faint trace of albumin was present only at the first examination, never any casts. Sugar was absent.

The figures from this one case compare favorably in a general way with those observed by Vannini in his five cases.

As yet too few practical clinical deductions can be obtained from the study of the metabolism in tetanus, because of the very little that has heretofore been accomplished in this direction, and compels us to trust to the future, with an increase of material and improvement of scientific investigations.

EPITHELIOMA OF THE VULVA.

A REPORT OF SIX CASES, WITH A REVIEW OF THE LITERATURE.*

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THERE are many essays on this subject, but the majority consist in a citation of cases with a very brief reference to the literature. Among the German and French writers, such men as Franke, Schwarz, and Maurel have produced excellent monographs, and from these works a considerable amount of the material for this paper has been derived. An attempt has been made to cover everything of importance in the entire literature, with a more minute analysis of the following 135 cases: Mayer,³⁷ 4; Arnott,¹² 2; Storer,⁵³ 1; Cushier,¹¹ 1; Aschenborn,³ 2; Küstner,³⁰ 5; Simmons,⁵² 2; Rupprecht,⁴⁹ 8; Manley,³⁴ 2; Janvrin,²⁷ 1; Maurel,³⁶ 27; Munde,⁴⁰ 1; Schmidt,⁵⁰ 2; Zeiss,⁵⁸ 1; Schwarz,⁵¹ 23; Ingerman-Amitin,²⁶ 7; Leech,³² 1; Hirst,²⁵ 2; Hart,¹⁹ 3; Henry,²⁰ 1; Mracek,³⁹ 1; Kelly,²⁹ 4; Franke,¹⁴ 16; Noble,⁴¹ 42 3; Butlin,⁸ 3; Congdon,¹⁰ 1; Peterson,⁴⁷ 4; Reed,⁴⁸ 1; Dittrick, 6.

The histories of the 6 cases that have been met with in the Lakeside Hospital will be given somewhat in detail:

* From the Gynecological and Pathological Departments of the Lakeside Hospital.