# CHAPTER XXIV.

## THE INTERNAL SECRETIONS IN THEIR RELATIONS TO PATHOGENESIS AND THERAPEUTICS (*Continued*).

### CONVULSIVE DISEASES DUE TO HYPOACTIVITY OF THE ADRENAL SYSTEM.

A suggestive fact bearing directly upon the disorders studied in this chapter, viz., tetany, tetanus, epilepsy, puerperal eclampsia, and rabies, is that many investigators have been led to conclude by experiments in which each organ was studied individually, that the adrenals, the pituitary body and the thyroid apparatus not only influence metabolism, but that they are also concerned with the destruction of toxic waste-products. Thus, in 1891, Abelous and Langlois[1] urged that the function of the adrenals was to "neutralize or destroy toxic substances produced or elaborated during chemical interchanges, and particularly those resulting from muscular work." In 1894 Lloyd Andriezen[2] concluded that "the pituitary gland exercises a trophic action on the nerve tissues, which, in more definite terms, means enabling them" . . . . "to destroy and render innocuous the waste-products of metabolism." As to the thyroid, it may be said to have been connected with both these processes almost since any function was ascribed to this gland. "According to one hypothesis," says Howell,[3] "the function of the secretion is antitoxic. In some way it antagonizes toxic substances supposed to be formed in the body in the course of normal metabolism." We have seen in a preceding chapter, that the labors of Vassale and Generali, Gley, Moussous, Jeandelize and others have conclusively shown that this applied to the parathyroids as well.

In the first volume (1903) and in several papers written since, I pointed out that the spasmodic and convulsive phenomena witnessed after removal of either the thyroid, adrenals

[1] Abelous and Langlois: Arch. de physiol. norm. et path., 5 série, vol. iv, pp. 269, 465, 1892.
[2] Andriezen: Brit. Med. Jour., Jan. 13, 1894.
[3] Howell: Trans. Congr. Amer. Phys. and Surgs., vol. iv, p. 70, 1897.





or pituitary should not be ascribed to the fact that absence of either of these organs prevented a direct action by their secretion or their cellular elements upon spasmogenic poisons, but that the seizures were caused by toxic waste-products, as all three of these organs formed part of the adrenal system which carried on the oxidation process through which these wastes would otherwise have been adequately catabolized.

Although over four years have elapsed since I urged this view, submitting considerable clinical and experimental evidence in its support, mere assumptions as to the pathogenesis of the group of disorders studied in this chapter still hold sway, while the appalling mortality of the acute diseases among the group continues unchecked. Of tetany, the simplest of the series, Osler says, in the last edition of his Practice (1905): "The nature of the disease is unknown." Ample testimony is available to show that a corresponding ignorance of the nature of the other diseases of the group prevails. Indeed, Joseph Collins,[4] a prominent neurologist, wrote recently: "We know very little more concerning the etiology, pathogenesis, and the clinical display of nervous diseases, organic and functional, than we did twenty years ago." This state of things will continue as long as neurologists will persist in ignoring the cardinal rôle of the internal secretions in nervous diseases.

The strength of the evidence submitted in this chapter to the effect that hypocatabolism is the underlying cause of the five diseases studied below is self-evident. Whether, as in tetany or the far more severe puerperal eclampsia, it be due to the formation of products of metabolism in excess of the quantity which the adrenal system can convert into benign and eliminable products; or to paresis of the adrenal system itself by tetanotoxin or the virus of rabies; or to functional torpor, inherited or acquired, of the same system as in epilepsy, the pathogenic agents (various intermediate products composing the poison) are the same, though the effects are materially influenced by the degree of toxicity of the blood, the efficiency of the test-organ, etc.

In the first volume and elsewhere I also submitted that the adrenoxin-laden plasma circulated in the axis-cylinders. Con-

[4] Joseph Collins: Monthly Cyclo. of Pract. Med., Feb., 1905.

siderable evidence has since sustained this view, as we have seen. This explains, which no one had done before, the presence of tetanotoxin in the axis-cylinders and its steady progress —as well as of methylene-blue and antitoxin—in these nervous structures.

Again, having urged that imperfect catabolism and inadequate functional efficiency of the adrenal system were the underlying cause of spasm and clonic convulsions, and in the presence of the striking beneficial effects of thyroid extract in experimental tetany, I laid stress on the pernicious influence of the bromides, chloral and other depressants, calling attention to the fact that, far from tending to cure, these drugs tended to kill. "They reduce, it is true," I wrote at the time,[5] "the excitability of the sensory elements, but they aid the accumulation of the spasmogenic toxics by inhibiting the oxidation process through which these are destroyed." Again, after calling attention to the hypothermia, the bromides and chloral provoked: "If the protective, curative element in these dread diseases is hyperoxidation, what may we expect of induced hypoxidation? The mortality ratio of rabies, tetanus and puerperal eclampsia treated on these lines answers that question."

Conversely, we will see in the following pages that in the *acute* diseases full doses of thyroid extract, of iodine, of the iodides, of biniodide of mercury, etc., of powerful adrenal stimulants, in a word, are curative. The paresis of the test-organ caused by the tetanotoxin and the rabic virus, and the inability of the organ to rise to the occasion in eclampsia impose the need of these large doses, the aim being to prevent the paroxysms by insuring a continuous destruction of the toxic wastes which incite them. In epilepsy, the object is the same; but small doses are alone needed here; the accumulation of toxic wastes being relatively slow, the aim is to supply the small surplus of oxygenation required, and to reduce by dietetic measures the products of metabolism formed.

On the whole, the picture submitted below of the pathogenesis of the dread diseases studied in the present chapter and the modus operandi of the various agents recommended, differ from any so far contributed except by myself. But I must

[5] Sajous: Jour. Amer. Med. Assoc., Feb. 4, 1905.



again urge that with the adrenal system as the fundamental mechanism of all processes involved, the relations between cause and effect appear in their true light, viz., that it is only by aiding the body's defensive resources that we can hope to master disease.

## TETANY.

SYNONYMS.—*Intermittent Tetanus; Little Tetanus; Tetanilla.*

**Definition.**—Tetany, a disorder characterized by painful tonic spasms, is caused by waste-products which, by provoking a marked rise of blood-pressure, cause capillary hyperæmia and hyperexcitability of all organs, including the spinal and peripheral nervous systems. A spasm occurs when this general excitability is suddenly increased by the appearance in the blood of an excess of auto-antitoxin, the result, in turn, of a defensive reaction of the adrenal system, and lasts until the spasmogenic poisons have been more or less converted into harmless and eliminable end-products.*

**Symptoms and Pathology.**—In some cases the spasms proper are preceded by *prodromata, i.e.,* tingling or numbness of the extremities, headache, nausea and vomiting, mental depression, vertigo, irritability, a vacant stare, and transitory blindness.

The *spasms* occur in the four extremities in the majority of cases and in the upper extremities in practically all other. The thumb is flexed in the palm, the fingers are bent at the metacarpo-phalangeal joint, but stiff beyond this limit, the wrist is flexed upon the forearm and the arm folded over the chest. In rare instances, the fingers close over the thumb. The spasms soon extend to the lower extremities; as a rule, these are stiff at the hips and knees, the feet being extended and the toes flexed. The facial muscles are often involved, causing locking of the jaws, as in tetanus, and the *risus sardonicus.* When the muscles of the neck, chest and back are the seat of spasm, the head may be thrown forward or backward, and opisthotonos may occur. The diaphragm and the laryngeal muscles are not infrequently included in the morbid process, causing marked dyspnœa. Stridulous respiration and cyanosis

* *Author's definition.*

may be provoked by the laryngospasm, a dangerous feature of this disorder. Pain in the contracted muscles and cutaneous hyperæsthesia are generally present. Among the phenomena less frequently observed are: œdema of the extremities, sweating, erythema, purpura and other eruptions, and anuria. The pulse is frequently accelerated, though the temperature is usually normal, and seldom exceeding in the exceptions 101° F. (38.3° C.).

The spasms proper may last but a couple of minutes, but often they succeed one another without complete relaxation during the intervals, so that the paroxysm is in reality a series of exacerbations of spasm lasting from ten to fifteen minutes. They may recur repeatedly in twenty-four hours during several days, weeks, and even months.

Several of the phenomena mentioned do not appear in the average text-book. The vacant stare was observed by F. M. Crandall.[6] C. P. Howard,[7] in a study of a large number of cases, states that "transitory blindness has been recorded by Kussmaul, Bouveret, Trevilian and Cunningham." Of trismus, Howard writes: "That this does occur in tetany as well as in tetanus must not be forgotten, as it is present in 10 of my series," *i.e.*, 68 cases, including 9 of his own. Again, he states that "spasm of the muscles of the neck, or of the back, or of both was present in 24 cases, and in several gave rise to well-marked opisthotonos." Finally, referring to the spasm: "While usually tonic in character, it may be clonic at the onset, and in some cases from this fact may be mistaken for epilepsy; though it should be borne in mind that in true epilepsy the tonic stage always precedes the clonic. A general convulsion occurred in 13 of my series, of which 9 were children." Tetany obviously embodies many of the characteristic symptoms of tetanus and epilepsy.

**Etiology and Pathogenesis.**—Tetany is primarily due to an accumulation in the blood of toxic waste-products which irritate the vasomotor and sympathetic centers. The general and marked vasoconstriction which occurs, causes the blood of the large deeper vessels to be driven towards, and accumulate in, the capillaries of the entire body.* As the brain and spinal cord are themselves rendered hyperæmic by this process, their irritability becomes so great that the slightest excitation from the periphery evokes a violent reaction.* The cutaneous sensory nerve-endings being likewise rendered hyperæmic,* they also become hypersensitive to external impressions, and a condition is produced in which reflex spasm may be brought on by external

* *Author's conclusion.*
[6] F. M. Crandall: Archives of Pediatrics, Dec., 1895.
[7] C. P. Howard: Amer. Jour. Med. Sci., Feb., 1906.



excitants which, under normal conditions, would have produced no reaction.* Hence* the muscular contraction produced by tapping over a muscle (Chvostek's symptom), or by pressure upon a large nerve or artery (Trousseau's symptom), the marked electrical excitability (Erb's symptom) and other familiar signs.

That some toxic is the spasmogenic agent is now believed by practically all observers. Bouchard, Gerhardt, Bouveret and Deric,[8] Carpenter[9] and others have ascribed it to intoxication of gastric origin; Ewald and Albu[10] to a toxic alkaloid of intestinal origin found in urine; Oddo and Sarles[11] and Oddo[12] to a toxin circulating in the blood.

As to the presence of hyperæmia, Tonnelier, Blondeau, Grisolle and Trousseau recorded cases in which they had found hyperæmia of the brain and meninges, and Weiss, Bonome, Cervesato and Szabo, and others in which poliomyelitis was present. R. Peters[13] in an exhaustive analysis of 77 cases, including 7 of his own studied microscopically, found the main lesions to be a small-celled infiltration with hæmorrhages, the latter occuring preferably between the ganglia and anterior roots, inflammation of the ganglia, and pachymeningitis. Peters ascribes the disease to leucomaines or ptomaines liberated by auto-intoxication, and which exert their morbid influence upon the nerve-roots. Degenerative lesions in the gray substance and most pronounced in the anterior horns have been observed by Weiss, Bonome and others.

The frequency with which mechanical irritability of the surface occurs is shown by the fact that it was present in all of 49 cases of infantile tetany studied by Ganghofner;[14] the Trousseau phenomenon was present in 28 of these instances. Romme[15] even ascribes the laryngospasm and facial phenomena to "reflex hyperexcitability of the cord and peripheral nerves."

The manner in which the sympathetic center is influenced is considered at length under "Tetanus," a kindred disease.

Tetany occurs in the course of many diseases. Prominent among these are: (1) various gastric and intestinal disorders; (2) infectious diseases, such as typhoid fever, variola, malaria, cholera, scarlet fever, measles, erysipelas, pertussis, pleurisy, bronchitis and influenza; (3) pregnancy and lactation; (4) uræmia and insolation; (5) violent excitement and exertion. In all these conditions, tetany is an accessory phenomenon, due, not to the autotoxins or bacterial toxins they add to the blood, but to a single class of spasmogenic agent in all cases, *i.e.*, toxic products of imperfect catabolism.*

These toxic wastes accumulate in the blood, because the

* *Author's conclusion.*
[8] Bouveret and Deric: Revue de méd., vol. xii, pp. 48, 97, 1892.
[9] Carpenter: Jour. Amer. Med. Assoc., Aug. 4, 1894.
[10] Ewald and Albu: "Autointoxication en des intestinal tractus," 1895.
[11] Oddo and Sarles: Marseille-médical, Oct. 1, 1894.
[12] Oddo: Revue de méd., vol. xvi, pp. 458, 573, 667, 749, 1896.
[13] R. Peters: Deut. Archiv f. klin. Med., Bd. lxxvii, S. 69, 1903.
[14] Ganghofner: Zeit. f. Heilkunde, Bd. xxiii, S. 244, 1902.
[15] Romme: Gaz. hebd. de méd. et de chir., Jan. 24, 1897.

adrenal system—including the thyro-parathyroid apparatus—though able to supply enough auto-antitoxin and thyroidase (which as opsonin sensitizes the poison) to convert all physiological wastes into benign and eliminable end-products under normal conditions, fails to increase its functional activity sufficiently when these wastes are produced with unusual rapidity (3d, 4th and 5th group), or when exogenous poisons such as those derived from the alimentary canal, or bacterial toxins (1st and 2d group), are added to the blood.* In the former case toxic intermediate wastes simply accumulate in the blood-stream; in the latter case, the exogenous poison or toxin, by utilizing for its own neutralization a given proportion of what auto-antitoxin is available, diverts a corresponding quantity from the physiological products of catabolism, the result being the same, *i.e.*, a gradual accumulation of toxic wastes, several of which are known to be spasmogenic.*

Tetany may also be caused by (1) certain drugs, alcohol, for instance, (2) rickets and (3) removal of the thyroid and parathyroids, and myxœdema; the disorder being due here to artificially produced deficiency of auto-antitoxin and thyroidase in the blood.* Thus, alcohol becomes oxidized at the expense of the blood's adrenoxidase and so reduces the quantitative efficiency of the latter that the auto-antitoxin formed is poor in this substance; as a result waste-products are imperfectly broken down, and toxic wastes accumulate*—provided the adrenal system fails to react. Rickets, a disease due to deficient nutrition of the bones owing to tardy development of the pituitary body, *i.e.*, of the adrenal center, is self-explanatory as a cause, since the resulting deficiency of adrenoxidase entails imperfect catabolism.* Removal of the thyroid and parathyroids accounts as readily for the tetany it provokes, since it is this organ's secretion, thyroiodase* (opsonin*), which sensitizes all substances to be catabolized, besides sustaining the functional efficiency of the adrenal center up to its normal standard.*

Briefly, notwithstanding the multitude of disorders with which tetany is associated it is invariably the result of an accumulation of toxic wastes in the blood,* except when caused by exogenous poisons.

* *Author's conclusion.*



Biedl[16] states that "the generally accepted view today (Pineles, von Frankl-Hochwart Chvostek) is that all forms of clinical tetany are of parathyroid origin." From my viewpoint this is due to the fact that removal or pathological destruction of the parathyroids deprives the thyroid secretion of its main antitoxic constituent.

We have seen that various authors ascribe tetany to toxins of gastro-intestinal origin. While this accounts theoretically for some cases, it fails to do so in the seven other groups enumerated, although the symptoms of the disorder are similar, though differing in intensity, in all cases. This points clearly to a common cause. The epidemic forms observed in Europe, by von Jaksch[17] and others, were in reality some obscure disorder, in the course of which tetany appeared as it does in many diseases. Tetany itself thus loses the epidemic character attributed to it by some. That several intermediate waste products capable of causing convulsions have been isolated will be shown in the articles on Tetanus and Epilepsy.

Even apart from my own views, the thyroid gland, including the parathyroids, is now regarded as serving to antagonize spasmogenic poisons. Thus Howard, referring to the investigations of Gley, Vassale, Generali, Halsted and MacCallum—all of which, beside others, have been reviewed in this work—states that "when these glands are removed, a poison which was formerly neutralized by them acts upon the central nervous system and produces tetany." MacCallum is also stated by Howard to have ascribed tetany to "the production of so much of this unknown poison that the normal parathyroids are insufficient to neutralize it." Conversely, Fleiner "regards the action of poisonous products of metabolism as of less importance than other factors," but Howard points out that "the great objection to Fleiner's theory is that it suffices only as an explanation for the gastric form of tetany." Even here it fails, for, as Howard correctly states, "Albu, Gumprecht, von Jaksch, Dickson and others have repeatedly failed to reproduce tetany by injecting into animals *untreated* gastric contents from cases of tetany." It is evident, therefore, that *not one* of the eight groups of disorders mentioned above is the spasmogenic agent, and that poisonous products of metabolism can alone be credited with this morbid rôle.

But how account for the marked clinical kinship between some cases of tetany and epilepsy? L. Pierce Clark,[18] after studying 150,000 epileptic seizures at the Sonyea Colony for Epileptics, concludes that "we must see the principle of pathogenesis in an initial toxin or auto-intoxication," *i.e.*, "an accumulation of waste-products."

When the accumulation of toxic wastes attains a certain degree which varies according to the sensitiveness of the test-organ, this organ awakens through the adrenal system a protective reaction.* The adrenals being stimulated, the proportion of adrenoxidase—and therefore auto-antitoxin—in the blood is increased temporarily.* The effect produced is apparently a morbid one, *i.e.*, a *spasm* or series of them, since the sudden increase of oxygen in the blood further excites the already hypersensitive nervous system, central and peripheral.

* *Author's conclusion.*

[16] Biedl: "The Internal Secretory Organs," p. 46, 1913.
[17] Von Jaksch: Zeit. f. klin. Med., Bd. xvii, Suppl., S. 144, 1890.
[18] L. Pierce Clark: Med. News, July 18, 1903.

The increase of auto-antitoxin compensates for this: It neutralizes not only the toxic wastes, but also the specific poison or toxin of the disease (typhoid, erysipelas, etc.) upon which tetany, an autonomous phenomenon, may be grafted.*

The spasms of tetany are, to a certain extent, therefore, an expression of auto-protective activity.* They occur partly because the augmentation of auto-antitoxin, which is the body's main safeguard in all diseases and the active agent in all febrile processes, happens to coincide with a condition of marked irritability of the central nervous system.*

This accounts for the fact that a period of improvement often succeeds a convulsion. The curative influence of thyroid extractives or thyroid grafting in the tetany following thyroidectomy points to the manner in which the toxic wastes are neutralized. By stimulating the adrenal center the proportion of antitoxin is increased—precisely as if the thyroid gland were still present. Thus, Hutchinson[19] and others found that thyroid extract increased oxidation, while Magnus Levy[20] and Scholz[21] observed that it increased the consumption of oxygen and the proportion of $CO_2$ excreted. As will be shown under Treatment, it is as effective in clinical tetany as it is after thyroidectomy.

**Treatment.**—The primary disease, that which, by depriving the blood of some of its auto-antitoxin, renders the accumulation of toxic wastes possible, should be eliminated whenever feasible. Practically all cases in adults are due either to some gastric or gastro-intestinal disorder, or to pregnancy and lactation. Gastric dilation is not infrequently observed and it is in this class of cases that death is apt to occur. An important feature of this condition is that it is directly due to insufficiency of the adrenal system: the blood being poorly supplied with adrenoxidase, the entire muscular system is relaxed, including the musculature of the stomach.* A similar condition prevails in pregnancy, the adrenal center being unable to insure neutralization of the waste-products of both mother and fœtus.*

Under these conditions, treatment of the tetany itself (besides any other measure that the concomitant disorder demands), *i.e.*, stimulation of the adrenal mechanism to increase the blood's auto-antitoxin, meets the needs not only of the tetany, but of the primary disorder also.* Again, when we consider that it is through an increase of auto-antitoxin that

* *Author's conclusion.*
[19] Hutchinson: Brit. Med. Jour., July 16, 1898
[20] Magnus Levy: Berl. klin. Woch., Bd. xxxii, S. 650. 1895.
[21] Scholz: Cent. f. inn. Med., Bd. xvi, S. 1041, 1069, 1895.



all exogenous and endogenous poisons are antagonized in the blood, it becomes apparent that all agents which increase the functional activity of the adrenal system tend to cure not only tetany itself, but its cause.* *Thyroid gland* (that available, which contains parathyroid) is thus indicated in all forms of tetany. Large doses have been found necessary; 5 grains (0.3 gm.) or more every three hours may be used at first, and gradually increased. *Parathyroid* is beneficial in some cases, but probably only the milder ones. (See also p. 741, vol. i.)

It is probable that the underlying cause of tetany in many cases is deficiency of thyroid secretion. Thus Gottstein[22] arrested tetany of twenty years' duration in a case of myxœdema. Yung, Breisach, Murray, Hutinel, Maestro[23] and Byrom Bramwell[24] have also reported cases of tetany or laryngospasm apparently devoid of hypothyroidia benefitted and even cured by thyroid extract.[25] Levy-Dorn[26] obtained striking results in a case following parturition, the spasm ceasing after the sixth dose. Other instances of this kind have been reported. This result obtains, however, only in cases in which the adrenal center responds to excitation; it may be too poorly developed to do so, as in some rachitic children, or it may have been so actively stimulated by the concomitant process, pregnancy for instance, that its efficiency cannot be raised further even by thyroid extract and the tetany persist.

As to the value of parathyroid extract, the question is still unsettled. Easterbrook[27] tried parathyroid extract in several cases, employing enormous doses in some; the only effect was a slight rise of blood-tension. MacCallum,[28] however, was able to arrest the symptoms produced by excision of the parathyroids by injecting the blood of a normal dog. The same observer and Davidson[29] found that an emulsion or extract, to produce its maximum effect, must be introduced into the veins in considerable quantity—a fact which they think tends to militate against its use in human beings, although it might be of use in cases due to partial adrenal insufficiency. This is sustained by the observation of Loewenthal and Wiebrecht that it was beneficial in some cases and not in others. The fact that the product of the parathyroids is but a constituent of thyroidase probably accounts for its relative inertness. In the light of my views it requires the secretion of the thyroid to acquire its physiological power.

In children gastro-intestinal disorders are likewise the primary exciting cause in the majority of cases. Purgation and attention to the diet sometimes suffice to arrest the spasms. *Thyroid gland* has also given good results in such cases after the alimentary canal had been judiciously treated. *Calomel,*

* *Author's conclusion.*
[22] Gottstein: Deut. Zeit. f. Nerven., Bd. vi, S. 177, 1895.
[23] Maestro: Rif. Med., vol. xii, Pt. ii, p. 468, 1896.
[24] Byrom Bramwell: Brit. Med. Jour., June 1, 1895.
[25] Cited by Jeandelize: "Insuffisance thyroidienne, etc.," 1903.
[26] Levy-Dorn: Therap. Monats., Bd. x, S. 63, 1896.
[27] Easterbrook: Lancet, Aug. 6, 1898.
[28] MacCallum: Med. News, Oct. 31, 1903.
[29] MacCallum and Davidson: *Ibid.*, Apr. 8, 1905.

which also stimulates energetically the adrenal center,* has been used advantageously every other day in $^3/_4$ grain (0.05 gm.) doses to prevent the formation of toxic substances.* *Saline aperients* are also useful in such cases. *Salol,* 5 grains (0.3 gm.), has been recommended for the same purpose. *Warm baths,* by drawing blood to the periphery and increasing (owing to the heat, which enhances the energy of all ferments) the proteolytic activity of its auto-antitoxin,* are very beneficial.

Oddo[30] found calomel very efficacious in the above dose, for the expulsion of intestinal toxic substances and their removal. With Hauser[31] he recommended lavage, but this is a difficult and dangerous procedure in tetanic children. Maestro observed that thyroid gland, administered raw or slightly cooked, 30 to 60 grains (2 to 4 gms.) daily, to children, rapidly diminished the intensity of the spasms and finally arrested them. Warm baths are recommended by many clinicians; the efficiency of ferments being raised by heat, the trypsin of the auto-antitoxin acquires increased activity; moreover, the congestion of the central nervous system is markedly relieved.

*Saline solution* is a useful adjuvant to increase the osmotic properties of the blood and thus facilitate the circulation of the auto-antitoxin.* It may be given orally in adults and by enema in children, large quantities being injected.

Kussmaul long ago suggested that the spasms were at least partly due to diminution of the body fluids—the theory of "dehydration" supported by other clinicians. It is mainly in severe types of tetany that the decinormal solution is effectual. Thus Gomez[32] obtained prompt results and finally recovery in cases in which the spasms included opisthotonos.

To control the spasms, 10-grain (0.65 gm.) doses of *bromide of sodium* usually suffice; such doses reduce the excitability of the vasomotor and sympathetic center just enough to diminish the cutaneous congestion without lowering the activity of the adrenal center.* If it fails to reduce the spasm *chloral hydrate* may be added to the bromide, also in 10-grain doses. In children the chloral may be given by enema. Additional measures to relieve the spasm are given in the article on Tetanus.

* *Author's conclusion*
[30] Oddo: *Loc. cit.*
[31] Hauser: Berl. klin. Woch., Bd. xxxiii, S. 782, 1896.
[32] Gomez: Rif. Med., vol. xvi, Pt. i, p. 207, 1900.



## TETANUS.

SYNONYM.—*Lockjaw.*

**Definition.**—Tetanus, a condition characterized by paroxysms of severe tonic spasm, is the terminal stage of an infection by a specific bacillus the toxin of which causes paresis of the test-organ. The functions of the adrenal system being inhibited, toxic waste-products accumulate in the blood which provoke an intense rise of blood-pressure and, as a result, capillary hyperæmia and hyperexcitability of all organs, including the spinal and peripheral nervous systems. A spasm occurs when this hyperexcitability is suddenly increased by the appearance in the blood of an excess of auto-antitoxin, the result, in turn, of a defensive reaction of the adrenal system, and lasts until both the specific toxin and the toxic wastes have been more or less converted into harmless and eliminable end-products.*

**Symptoms and Pathology.**—The tetanic paroxysms appear from a few hours to two weeks after the introduction of the specific agent of tetanus into the tissues. The attack is sometimes preceded by chilly sensations, hypothermia, lassitude, yawning, and in traumatic cases by some tenderness and muscular twitchings in the neighborhood of the wound.

The attack itself begins by more or less marked rigidity and perhaps slight pain of the muscles of the jaws, neck, tongue and œsophagus, the patient soon finding it difficult to swallow and then impossible to open his mouth. This stiffness gradually invades the entire body, *i.e.,* the muscles of the back, abdomen and legs, and the patient finally becomes as stiff as a board. In some cases the spasm occurs in certain groups of muscles earlier than in others and the body may be bent to one side or the other, backward—opisthotonos—or forward. The facial muscles may also contract irregularly, causing distortion of the features; the eyebrows may be raised and the angles of the mouth elevated, causing the grin of tetanus, *i.e.,* the *risus sardonicus.* The paroxysms, at first comparatively painless, become extremely severe, the patient being often in drenching sweat; but fortunately they do not generally last

* *Author's definition.*

longer than fifteen seconds. They may be provoked by the slightest touch, a breath of air, noise, etc.

When the muscles of respiration and the diaphragm take a very active part in the spasm, the respiration becomes hurried and short and the patient may die of asphyxia. The heart may likewise be inhibited through excessive constriction of the coronaries,* and its action become very weak, irregular and finally arrested. Although the temperature may rise moderately during the seizure, it sometimes becomes high—110° F. (43.3° C.) on the approach of death. Most cases die within the first few days, but some may endure much longer—weeks even.

**Pathogenesis.**—Tetanus is due to the accumulation in the blood of certain poisons which cause marked irritation of the sympathetic and vasomotor centers.* The propulsive activity of the arterioles is not only enhanced to a marked degree by the exaggerated sympathetic impulses, but the irritation of the vasomotor center, by provoking excessive and general vasoconstriction, causes the deeper vascular trunks to drive a part of their blood into the peripheral capillaries, including those of the spinal cord and skin.* The spinal reflex centers being thus rendered excessively irritable and the cutaneous sensory terminals correspondingly sensitive, a condition is produced in which a spasm may be brought on at any moment by the slightest exciting cause, a touch, a breath of air, a slight noise, etc., or some endogenous excitant.*

The blood-pressure was found elevated by Tauber[33] not only during spasms, but also during the intervals. The arterial tension is so great in some cases that rupture of the capillaries may be caused by the blood forced into them. Thus, Molle[34] observed hæmorrhage in tetanus. Marinesco[35] found diffuse hæmorrhages in the gray substance of the spinal cord, especially in the anterior horns. Hunter[36] noted marked dilation of the spinal vessels, coupled with infiltration and miliary hæmorrhages; Matthes[37] also found in the spinal cord extensive hæmorrhages and disseminated smaller hæmorrhages, coupled with "enormous" enlargement of all the small blood-vessels—a condition which the author ascribes to hyperæmia, and not to the tetanus poison. Of course, all muscles, including those of the vessels, being abnormally contracted during spasm, the blood-pressure is higher during the latter than during the intervals, but the fact remains that the blood-pressure is high during the entire course of the disease and that this is due to irritation of the spinal cells.

* *Author's conclusion.*
[33] Tauber: Wiener klin. Woch., Bd. xi, S. 747, 1898.
[34] Molle: Bull. méd., vol. x, p. 135, 1896.
[35] Marinesco: C. r. Soc. de biol., 10 série, vol. iii, p. 726, 1896.
[36] Hunter: Brit. Med. Jour., Aug. 7, 1897.
[37] Matthes: Deut. Zeit. f. Nerv., Bd. xiii, S. 464, 1888.



As to the participation of the sympathetic center in the process, we have seen that Cyon produced spasm by exciting this organ, *i.e.*, the seat of the general sympathetic center, as I have pointed out. These fibers, after leaving the pituitary and the nucleus above, pass posteriorly along the walls of the third ventricle. This accounts for the muscular movements noted by Flourens, Bechterew, Weber, Ferrier and others on exciting the walls of the third ventricle. Ziehen,[38] moreover, found that removal of the hemispheres in rabbits and excitation of the remaining structures, including the corpora quadrigemina, caused prolonged tonic spasm. Prus[39] then found that when the pyramids had been divided, the spasmogenic impulses passed by way of the base, *e.g.*, the tegmentum and pons, an observation confirmed by Bischoff,[40] Hering and others.

Hering,[41] in experiments which included twenty monkeys, ascertained that after division of the pyramids in the latter animal it was impossible "to inhibit a tonic spasm in the isolated extremity." In an extensive series of experiments, Nino Samaja[42] recently showed, in fact, that in the higher mammals *tonic* convulsions were "exclusively" due to impulses from the *base* of the brain, the path, we have seen, of the sympathetic filaments derived from the pituitary body.

The presence of marked hyperæmia of the spinal system is generally recognized. Thus Ewing,[43] referring to the spinal cord of a case examined by him, states that "the capillaries were everywhere distended with blood and a few minute extravasations were found in the floor of the fourth ventricle."

When the accumulation of toxic wastes in the blood exceeds a certain limit, the test-organ incites a protective reaction through the adreno-thyroid center.* A large quantity of auto-antitoxin suddenly invading the blood, the existing hypersensitiveness of all nervous elements, central and peripheral, is increased, owing to the increased rapidity of metabolism, and a spasm occurs.* Indeed, the spasms should not be regarded as constituting the disease as the term "tetanus" suggests; they represent a *terminal phase of the disease,* when the accumulation of poisons in the blood has become so great that a supreme physiological effort is necessary to destroy them.* Each spasm represents such an exacerbation of protective activity.*

The increase of auto-antitoxin in the blood being itself paroxysmal, as in all convulsive disorders, the erethism and sensibility of the spinal and cutaneous nerve-cells are also paroxysmal. Yet the paroxysm is not due to direct excitation, by the auto-antitoxin, of the cerebro-spinal cellular elements; these are merely rendered still more irritable than before.* The

* *Author's conclusion.*
[38] Ziehen: Deut. med. Woch., Bd. xiv, S. 604, 1888.
[39] Prus: Wien. klin. Woch., Bd. xi, S. 857, 1898.
[40] Bischoff: *Ibid.*, Bd. xii, S. 960, 1899.
[41] Hering: *Ibid.*, Bd. xii, S. 831, 1899.
[42] Nino Samaja: Rev. méd. de la Suisse rom., Mar. 20, 1904.
[43] Ewing: Arch. of Neur. and Psych., vol. i, p. 263, 1898.