

the form of urea was markedly lower than during normal pregnancy. Whitney and Clapp<sup>255</sup> confirmed this fact experimentally and clinically. Williams states that while, during an eclamptic attack, there is nearly always an abundance of albumin, often blood and tube-casts, the termination of the convulsions is marked, in favorable cases, by a rapid increase in the amount of urine and urea, together with a decrease in the amount of albumin."

**Treatment.**—MEASURES CALCULATED TO PREVENT ECLAMPTIC SEIZURES.—In view of the foregoing evidence, the importance of frequent examination of the urine is self-evident: at least once a month during the first six months and every other week thereafter, the patient being instructed to notify her accoucheur should headache, disturbance of vision, œdema, or jaundice appear—all symptoms of beginning toxæmia. The urine passed in the twenty-four hours, which will probably be found highly colored and scanty, should be measured, and the total output of albumin and urea estimated by Esbach's albuminometer and Doremus's ureometer.

Although the addition of the foetal wastes to those of the mother suggests that an excess of urea should be found, obstetricians are content with a normal output of urea (20 to 24 grams daily) even if a slight amount of albumin be present. Considerable albumin and a diminution of the urea excreted, however, betoken danger, and the patient should at once be restricted to *milk* (which serves both as food and diuretic), two quarts at least to be taken in the twenty-four hours, and all the water she can drink. When this does not procure the desired result, a decrease of albumin, a rise of urea-ratio and free diuresis, the daily use of *saline purgative* and *hot-pack* or *sweat-bath* should be resorted to.

An *exclusive milk diet* is recommended by Williamson and other American obstetricians, and by most French authorities, Charpentier, Tarnier and others. Charpentier,<sup>256</sup> in fact, to avoid all risk, orders it as soon as the urine contains the slightest trace of albumin, which would mean that about 50 per cent. of pregnant women should at one time or another be submitted to it. Féré<sup>257</sup> and Tarnier (whose experience has been extensive) had never seen at the time of their report a case of eclampsia in a patient who had subsisted for eight days on an absolute milk diet. As Féré observes, it does not always counteract the albuminuria or the œdema, but it averts toxic symptoms. This is accounted for by the conclusion I have submitted that the two former symptoms, when not marked, are not necessarily pathological, their persistence denoting that the patient's blood is rich in adrenoxidase.

<sup>255</sup> Whitney and Clapp: Amer. Gynecology, Aug., 1903.

<sup>256</sup> Charpentier: Arch. de tologie et de gynéc., vol. xx, p. 509, 1893.

<sup>257</sup> Féré: L'obstétrique, vol. i, p. 485, 1896.

If no improvement occur in the excretory phenomena and the headache and visual disturbances persist; or if drowsiness, hebetude and other symptoms previously enumerated as denoting irritation of the vascular centers appear, the likelihood that an attack of eclampsia is near at hand is very great. When this stage is reached, obstetricians usually induce premature labor, the life of the unborn child being sacrificed. According to my interpretation of the pathogenesis of the convulsions, other means are available, besides those just outlined, to prevent the attack of eclampsia.

The use of *saline solution* is indicated before as well as during the eclamptic period, since it is known to enhance the antitoxic activity of the blood by increasing its fluidity and its osmotic properties.\* When the absolute milk diet is not increasing the excretion of urea, therefore, sodium chloride should be added to the milk in the proportion of 50 grains (3.3 gms.) to the pint,\* the patient being directed to drink water at stated intervals. Often in these cases, there is fecal retention, notwithstanding daily evacuations. *Rectal irrigation* with large quantities (one to two gallons) of warm (110° F., 43.3° C.) saline solution is very valuable in all cases.

The experimental researches of Von Fodor, Blumenthal, Calabrese, Löwy and Richter and others have conclusively demonstrated that the antitoxic powers of the blood are inhibited by a diminution of its salts, while Jacques Loeb has shown that sodium chloride was essential to the life of the cell. Its beneficial effect during the eclamptic stage, even in apparently hopeless cases, is well known. As stated by Allen,<sup>258</sup> "it is impossible to appreciate its advantages unless one has watched its results." The taste of milk is improved rather than impaired by the quantity of salt mentioned. The effects of thyroid extract are given below. The use of high rectal injections, especially of saline solution, is generally recognized.

If these measures do not procure the desired result, the patient should remain in bed to reduce the proportion of sarcolactic acid eliminated by the muscular tissues into the lymph and blood, thus counteracting the only remaining poison-producing factor, namely, muscular exertion.\* The absolute milk diet being continued, *thyroid gland* should be given in doses of 3 to 5 grain (0.2 to 0.3 gm.) doses every three hours, the object being to stimulate the adrenal mechanism and increase

\* *Author's conclusion.*

<sup>258</sup> Allen: Amer. Jour. of Obstet., May, 1899.



the antitoxic activity of the blood.\* *Oxygen* inhalations are indicated in this connection, to hasten the conversion of the adrenal secretion into adrenoxidase.\*

The advisability of avoiding muscular exertion is well shown by the experiments of Mossaglia,<sup>250</sup> who found that dogs deprived of some of their parathyroids had typical convulsions after being fatigued. He emphasizes the fact that a woman threatened with eclampsia is more prone to an attack after being fatigued. We have seen that Vassale observed marked eclampsia during pregnancy in dogs deprived of their parathyroids, and that large doses of parathyroid arrested the attack.

Nicholson<sup>250</sup> introduced this treatment on the well-grounded plea, based on Lang's observation that the thyroid was enlarged, and his own that during eclampsia this phenomenon did not occur, that a deficient supply of iodothyron entailed a corresponding inadequate destruction of nitrogenous wastes. Although he believed that the antitoxic action of the thyroid secretion was direct and that the poison acted directly on the blood-vessels also—both untenable conclusions—the fact remains that the object—destruction of the spasmogenic poisons—was attained in the four cases reported. The doses ranged from 5 to 10 grains (0.3 to 0.6 gm.). In the first case, the seizures had begun; in the second there was slight general œdema and albuminuria; in the third the general œdema included the face, the urine was nearly solid, there was headache and dimness of vision. The fourth case was similar. Nicholson's observations have been confirmed by several obstetricians—but all after the convulsions had begun. Frühinsholz and Jeandelize<sup>251</sup> likewise advised the use of thyroid extract.

The inhalation of oxygen has been found of value even without thyroid extract; hence its probable efficiency with an increase of adrenal secretion in the blood-stream.

Simultaneously, if need be, the irritability of the general vasomotor center may be reduced by using drugs which are known to prove beneficial during the convulsions, and which are, therefore, all the more indicated in the pre-eclamptic stage.\* *Veratrum viride* is one of these; by inducing relaxation of all the arteries of the body it causes accumulation of the blood in the large central vessels, and by thus diminishing the cerebral hyperæmia tends to prevent the impending seizure. It may be given in 20 to 30 drop doses of the tincture (1905 U. S. P.) every two hours until the pulse becomes softer and slower, but larger doses are required in threatening cases to obtain this result. The physiological action of the *bromides* and *chloral* is similar to that of *veratrum*, we have seen, but their action is more uncertain.

The use of *veratrum viride* does not prevent that of thyroid

\* Author's conclusion.

<sup>250</sup> Mossaglia: Gazz. degli Ospedali, Sept. 2, 1906.

<sup>250</sup> Nicholson: Brit. Med. Jour., Oct. 11, 1902.

<sup>251</sup> Frühinsholz and Jeandelize: Presse médicale, Oct. 25, 1892.

extract, since each drug acts on a different center. The former should not be used hypodermically, however, in the pre-eclamptic period, since the reflex irritation produced by the needle and fluid may precipitate a seizure.

Wood, we have seen, says that *veratrum viride* bleeds the patient into his own vessels—a desirable effect under present conditions. Thayer<sup>252</sup> laid stress on the fact that during puerperal convulsions, a "peculiar tolerance" of *viride* existed, officinal doses having no effect. This is due to the great erethism of the vasomotor center; hence the need of full doses in the pre-eclamptic period. Edgar<sup>253</sup> considers it "the most certain remedy at our command for controlling the spasms temporarily, or even permanently." Norris, Hirst,<sup>254</sup> Jewett<sup>255</sup> and other obstetricians of large experience recommend it highly in convulsions. That it should be as useful to *prevent* convulsions, while the thyroid extract is causing destruction of the toxic wastes in the blood, is obvious.

MEASURES CALCULATED TO ARREST THE ECLAMPTIC SEIZURES.—If, notwithstanding the foregoing measures, eclampsia occurs, efforts to eliminate the poison and arrest the convulsions should even now be made before sacrificing the child by emptying the uterus. The irritability of the vasomotor center is best controlled, we have seen, by means of *veratrum viride*, 40 minims (3.6 gm.) of the tincture (1905 U. S. P.) may now be given hypodermically. Pending the vasodilating influence of this remedy, the convulsions may be held in check, if absolutely necessary, by means of a few whiffs of *chloroform* (an undesirable agent, since it irritates the vasomotor center) freely diluted with air. *Hypodermoclysis* should then be resorted to, one pint of saline solution at 110° F. (43.3° C.) being injected slowly beneath each breast. This may be repeated if necessary. Many experienced obstetricians practice *venesection* before using the saline solution, and find it of material aid, especially in plethoric or cyanotic women. To promote diaphoresis, the *hot pack* is generally recommended, and is much safer than *pilocarpine*. *Thyroid gland* is also indicated during this stage, but in full doses. *Iodine*, in large doses, may serve to replace thyroid extract if the latter is not available. (See also p. 784.)

The cases in which Norris found *veratrum viride* most useful were those with a full, rapid and high-tension pulse. Cotret<sup>256</sup> injects 20 drops, and the same quantity in 30 minutes if the pulse is not reduced.

<sup>252</sup> Thayer: Boston Med. and Surg. Jour., Apr. 1, 1897.

<sup>253</sup> Edgar: Therap. Gaz., Aug. 15, 1901.

<sup>254</sup> Hirst: *Ibid.*

<sup>255</sup> Jewett: Amer. Med. Digest, Feb. 15, 1888.

<sup>256</sup> Cotret: Rev. médicale du Canada, vol. vi, pp. 215, 230, 1902.



In one case he thus injected 400 drops, saving the case. E. P. Davis injects 40 minims (1905 U. S. P.) every hour until it falls below 90 and its tension is decidedly lessened. Hirst, who gives 60 to 80 drops (1905 U. S. P.) as the first dose, has seen it reduce the pulse to 60 in a few minutes; as long as it remained at that rate no convulsions occurred. Laphorn Smith<sup>267</sup> obtained subsidence of the blood-tension with 20 to 25 minims after other familiar remedies and even blood-letting had failed.

The beneficial influence of saline solution is well illustrated by the fact that in the Glasgow Maternity the mortality, according to Jardine,<sup>268</sup> has been reduced from 47 per cent. to 17 per cent. since this measure has been introduced. One drachm of sodium chloride to the pint of water at 110° F. (43.3° C.) is the solution employed, the site of the infusion being covered with towels wrung out of hot water.

Besides the pre-eclamptic cases treated by Nicholson, cases in which the seizures had developed and in which thyroid or parathyroid extract was successfully employed, have been reported by Macnab,<sup>269</sup> Baldowsky,<sup>270</sup> Vassale<sup>271</sup> and others, the last-named author having used later,<sup>272</sup> and with equal success, parathyroid extract.

Thyroid extract in large doses is recommended by Nicholson, Fothergill, Sturmer<sup>273</sup> and Lobenstine.<sup>274</sup> The latter gave it in 20-grain doses (1.3 gm.) per rectum several times in the twenty-four hours.

Acting upon my suggestion<sup>275</sup> that iodine should prove efficient in such cases, Somers<sup>276</sup> used doses sufficient to produce iodism of a preparation containing a large proportion of free iodine successfully. This indicates that this halogen can be used advantageously when fresh thyroid extract cannot be obtained. I prefer the iodides of sodium and potassium in large doses. It may also be administered per rectum with saline solution.

*Morphine* injections are advocated by some, but the benefit produced is an artificial one; the arterioles being constricted, the peripheral circulation is hampered and the cortical hyperæmia is reduced. The arteries are dilated behind their arterioles, by the accumulated blood; hence, the belief that it causes vasodilation. The arterioles of the skin and kidneys being likewise constricted, their excretory functions are inhibited.\* It should not be used, therefore, when the kidneys are at all diseased. It is far more efficacious, as shown below, when administered with chloral hydrate.

Francis<sup>277</sup> lost two cases out of five under morphine. Conversely, Fitzgerald<sup>278</sup> reports five cases, of which two, treated by chloroform and delivery, died, while the three others, in which morphine was used with-

\* Author's conclusion.

<sup>267</sup> Laphorn Smith: Montreal Medical Journal, Jan., 1902.

<sup>268</sup> Jardine: Edinburgh Med. Jour., July, 1903.

<sup>269</sup> Macnab: Jour. of Obstet. and Gynec. of Brit. Empire, Nov., 1904.

<sup>270</sup> Baldowsky: Vratsh, vol. xi, 1904.

<sup>271</sup> Vassale: Riv. Crit. di Clin. Med., Mar. 4, 1904.

<sup>272</sup> Vassale: Arch. Ital. di Biol., vol. xliii, p. 177, 1905.

<sup>273</sup> Sturmer: Brit. Med. Jour., Apr. 16, 1904.

<sup>274</sup> Lobenstine: Bul. N. Y. Lying-in Hosp., Dec., 1905.

<sup>275</sup> Sajous: Jour. Amer. Med. Assoc., Feb. 4, 1905.

<sup>276</sup> Somers: Western Med. Review, June, 1904.

<sup>277</sup> Francis: Brit. Med. Jour., Jan. 11, 1902.

<sup>278</sup> Fitzgerald: *Ibid.*, Nov. 24, 1900.

out delivery, lived. Veit<sup>279</sup> also recommends morphine, but when renal disease is not present—in accord with Tyson,<sup>280</sup> Reynolds Wilson<sup>281</sup> and others. Hoig<sup>282</sup> uses it only when there is free diuresis. He rightly avoids it also during the comatose state between seizures. Edward P. Davis<sup>283</sup> advises against its use, especially in large doses.

*Chloral* acts much as does veratrum viride, but, unlike the latter, it reduces the sensitiveness of the adrenal center besides controlling the irritability of the vasomotor center. While relieving the cortical hyperæmia, therefore, it tends to reduce the antitoxic properties of the blood.\* The *bromides* have a similar action, when the doses are sufficiently large to control the convulsions.\* As a temporary resource, however, chloral may be used advantageously when well diluted with water, by the mouth, or by rectal injections when the patient cannot swallow.

While the majority of European obstetricians consider chloral too depressing, Goodell, Hirst, Charpentier and other experienced observers advocate its use: Frazer<sup>284</sup> administered it per rectum, 1 drachm (4 gm.) being used for each enema, in 49 cases, and lost but two. Commandeur<sup>285</sup> contends that its rectal use is defective: it is not well retained and absorption is uncertain. Orally, when each 15 grains given is dissolved in at least 4 ounces (120 gms.) of water, it is well borne, and completely absorbed. Hallowes<sup>286</sup> reported four cases in which the injection per rectum of 60 grains (4 gms.) in 1 ounce (28 gms.) of water gave prompt relief.

*Morphine and Chloral.*—Combined, these two agents are far more useful than when given alone. Morphine being capable of stimulating both the adrenal center and the sympathetic center, it offsets the untoward action of chloral on the former, but not its depressing action on the vasomotor center. The chloral, therefore, tends to deplete the brain, *i.e.*, the cortex, of its excess of blood, while the morphine by constricting the arterioles, still further reduces the quantity of blood admitted to the cerebral capillaries.\*

This accounts for the results recorded by Stroganoff,<sup>287</sup> *viz.*, a mortality of 5.4 per cent. out of 92 cases observed by him. He injects  $\frac{1}{8}$  grain (0.01 gm.) morphine, and repeats the dose in one hour or earlier if the patient is restless. Two hours later he gives chloral per rectum, 30 to 45 grains (2 to 3 gms.) in aqueous solution, and repeats it at

\* Author's conclusion.

<sup>279</sup> Veit: Festsch. f. C. Rüge, 1896.

<sup>280</sup> Tyson: Gaillard's Med. Jour., Aug., 1891.

<sup>281</sup> Reynolds Wilson: Annals of Gynec. and Pediat., May, 1892.

<sup>282</sup> Hoig: Canadian Practitioner, July, 1900.

<sup>283</sup> E. P. Davis: Therap. Gaz., Dec. 15, 1899.

<sup>284</sup> Cited by Robbins: Amer. Lancet, Jan., 1888.

<sup>285</sup> Commandeur: Semaine méd., vol. xxii, p. 328, 1902.

<sup>286</sup> Hallowes: Lancet, July 13, 1901.

<sup>287</sup> Stroganoff: Vratsh, Sept. 16, 1900.



intervals of 4, 6, and 8 hours, unless the patient be resting quietly. Chloroform is used exceptionally—only in severe convulsions, pending the action of the morphine and chloral. The rectal and subcutaneous use of saline solution is deemed an important feature of the treatment. The author *did not have to induce labor in a single instance.*

If the foregoing measures prove unavailing, the uterus should be emptied. The precautions resorted to in epilepsy to prevent wounding of the tongue, etc., during the convulsions, are, of course, as applicable in eclampsia.

## RABIES.

SYNONYMS.—*Hydrophobia; Lyssa.*

**Definition.**—Rabies, a disorder characterized by violent tonic spasms with, in some instances, clonic convulsions, is the terminal stage of an infection by a specific virus which causes progressive paralysis of the test-organ. The functions of the adrenal system becoming gradually weaker, toxic wastes accumulate in the blood to a sufficient degree, after weeks or months, to cause a marked increase of vascular tension. As an excess of blood is thus driven into all capillaries, including the cerebro-spinal nervous elements, these are rendered hyperexcitable. The spasms occur when this hyperexcitability is suddenly enhanced by the appearance in the blood of considerable auto-antitoxin, due to a defensive reaction of the adrenal system evoked by the blood when it becomes sufficiently toxic to irritate violently the test-organ notwithstanding the paralyzing influence of the virus.\*

*Lyssophobia* or *Pseudo-rabies*, a morbid fear of hydrophobia in persons who have been bitten by animals supposed to be rabid, consists of a group of symptoms resembling true rabies, but including manifestations, such as attempts to bite, bark, etc., which are popularly thought to belong to rabies.

**Symptoms and Pathology.**—After a period of *incubation* varying from one week to three months, and in rare cases extending beyond this length of time, the *premonitory symptoms* appear. At first they resemble those of other diseases, irritability, anorexia, insomnia, depression and general malaise. Slight headache and rigors with some stiffness and even pain in the muscles of the neck, back and shoulder and arms are frequently

\* Author's definition.

complained of. The tongue is coated, the breath offensive, and the pupil is dilated. There may be slight fever, but in most cases the temperature is normal, and hypothermia is occasionally present. If the patient attributes his condition to the bite, brooding over its consequences may lead to melancholia and influence greatly the symptomatology of the second period of the disease. The wound, usually healed soon after the receipt of the injury, may be the seat of darting pains, become inflamed along, perhaps, with neighboring lymphatic glands.

Although occasionally rabies occurs long after the injury, most cases in which it appears beyond four months are not sustained by control inoculations. Bradford<sup>288</sup> states that "the incubation period in the human subject lies between 20 to 60 days, and it is exceedingly rare to have it appear after 3 months, and 6-months' incubation is practically unknown." As to the presence of low temperature, Sir Thomas Smith<sup>289</sup> observed a case which on admission had a temperature of 95° F. (35.50° C.) and a pulse of 56. Anders<sup>290</sup> observed two cases in which the dread of the disease after bites resulted in persistent melancholia.

The *spasmodic* stage is initiated by the symptoms due to excessive reflex irritability of the pharynx, larynx and œsophagus, the act of swallowing provoking reflex spasm of their muscles, and therefore intense dyspnoea owing to closure of the glottis. At first the difficulty is surmounted, but the spasms finally become so intense that they inspire extreme terror, and the sight of water, by suggesting the act of deglutition, is sufficient to bring on a distressing seizure. Hence the term "hydrophobia," a misnomer, since it is the spasm that is feared. The patient is nevertheless extremely thirsty and sometimes controls himself sufficiently to drink; milk is taken more readily than water under these conditions, especially if given in a covered vessel. In some cases, deglutition is impossible and the liquid regurgitates by the mouth and nose. Even the saliva, which in rabies is viscid, tenacious and secreted in greatly increased quantity, causes spasm when swallowed, and is expectorated, sometimes in its normal state, sometimes mixed with froth, owing to the churning it receives in the mouth—the so-called "frothing at the mouth."

The mucous membranes are not alone in a state of exalted irritability; as in tetanus, there is general hyperæsthesia of the skin, and the special senses become so acute that a slight

<sup>288</sup> Bradford: *Lancet*, Mar. 3, 1900.

<sup>289</sup> Sir Thomas Smith: *Practitioner*, Jan., 1898.

<sup>290</sup> Anders: "Practice of Med.," seventh edition, p. 358, 1905.



touch, a mere draught, a noise, etc., suffice to provoke a paroxysm. The orificial tissues, those of the anus for instance, are quite as sensitive, even rectal feeding causing spasm. Nor are the muscles of the upper respiratory and alimentary tracts alone involved in these seizures; the entire muscular system, including both the voluntary and involuntary muscles, may, as in tetanus or even in epilepsy, undergo violent contraction. The muscles of mastication are, in most cases, alternately locked and relaxed, causing the snapping which popular imagination has interpreted as efforts to bite. In truth, the patient, who is relatively quiet and able to speak rationally (at least in the earlier part of the convulsive stage), during the interval between the spasms is usually solicitous about those who minister to his wants. Rolling of the eyes and head, throwing of the limbs from side to side, etc., as in epilepsy, are also witnessed in some instances.

As the case proceeds, the mental excitement increases, the patient talking incoherently. This often lapses into the so-called "furious" stage, during which the patient is subject to waves of maniacal delirium, as it were, attended with delusions and hallucinations of a frightful nature. This coincides with an elevation of the temperature, reaching in some cases 105° F. (40.5° C.), a bounding, tense and rapid pulse, flushed face and eyes, and sometimes cyanosis. The pulse may become small and irregular during a spasm developed during this stage—a danger signal of oncoming cardiac (coronary) inhibition\* and sometimes of immediate death.\* Glycosuria and albuminuria are also observed during this stage.

The period of excitement finally passes into one of comparative quietude. The patient is then able to swallow with less trouble and may be thought to be recovering. But it is in reality the onset of the lethal or *paralytic period*; the cardiac action becomes weak and irregular, and the respiration shallow and rapid. The patient then gradually lapses into unconsciousness and coma, dying by syncope or in the midst of a terminal tetanic spasm. Death usually occurs within the four days following the onset of the convulsive period, but occasionally the patient lasts much longer.

\* Author's conclusion.

In rare cases, usually in neurotic or debilitated subjects or after multiple lacerations, the phenomena are all of the paralytic type. After the usual premonitory symptoms, dysphagia and attacks of spasmodic dyspnoea appear, soon followed by coldness, anaesthesia and torpor of the extremities, especially the lower. Paralysis follows and gradually becomes general, the lethal course described above then progressing rapidly.

The resemblance of rabies to tetanus is not only very marked, but tetanus is sometimes attended with distinct hydrophobic symptoms. In two cases reported by Roberts<sup>291</sup> and Van Spanje,<sup>292</sup> both in gardeners, in which infection occurred through slight wounds of the face from pointed sticks, the phenomena were clearly those of rabies. Anders and Morgan<sup>293</sup> refer to a case of tetanus reported by J. W. Ward, in which the diagnosis of hydrophobia was maintained several days. The paralytic form of rabies, that observed also in inoculated guinea-pigs and other animals, the rabbit, mouse, etc., is another point of similarity with tetanus. As to death occurring beyond the usual four days, Sweeney and Denny<sup>294</sup> refer to a case in which death occurred on the fourteenth day following the onset of the rabic symptoms. These authors correctly interpret what a study of a large number of carefully described cases indicates, when they remark: "The exaggerated picture of rabies in the mind of the laity and of physicians who have carelessly read text-books on the subject is never met with in actual practice. The barking, biting, crawling on all-fours and other extravagant symptoms belong rather to the spurious or hysterical type of the disease." In a case of the latter kind described by Fabricius,<sup>295</sup> the patient tried to bite, but he was clearly reproducing his conception of what a rabid man should do—though in the midst of a sharp attack of alcoholic delirium from which he promptly recovered.

**Etiology and Pathogenesis.**—Rabies is due to the presence in the blood of a poison which violently irritates the vasomotor and sympathetic centers.\* The resulting intense constriction of all arteries causes all the capillaries of the body to become correspondingly engorged by the blood forced into them, and the spinal (and in some cases the cortical) cells being thus rendered hyperæmic, they become, as in tetanus, excessively irritable.\* As the sensory terminals of the peripheral mucous membranes and skin are also rendered hypersensitive through hyperæmia of their capillaries, the least irritation of the surface provokes a violent reflex spasm.\*

The pharynx, larynx and œsophagus are the first to react,

\* Author's conclusion.

<sup>291</sup> Roberts: *Lancet*, July 11, 1891.

<sup>292</sup> Van Spanje: *Nederlandsch Tijdschrift voor Geneeskunde*, vol. xxvii, p. 397, 1891.

<sup>293</sup> Anders and Morgan: *Jour. Amer. Med. Assoc.*, July 29, 1905.

<sup>294</sup> Sweeney and Denny: *Northwestern Lancet*, Apr. 1, 1896.

<sup>295</sup> Fabricius: *Med. Record*, Dec. 28, 1895.



because it is to this region that an external irritant is applied when ingesting fluids or food. Irritation applied elsewhere, the surface, the anal aperture, etc., likewise produces spasm in these structures and in them only at first because they are nearest to the seat of the general centers primarily irritated, those in the pituitary body.\*

The presence of marked vascular engorgement has been emphasized by a large number of observers. Van Gehuchten and Nélis,<sup>296</sup> for instance, found "everywhere in the nervous system a vascular dilatation" and in some, "general thrombosis of the small veins with an excessive perivascular infiltration." Babès<sup>297</sup> had previously laid stress on this condition. In a case controlled by inoculations in rabbits by Ravenel, and reported by Krauss,<sup>298</sup> Wadsworth found "severe congestion of the cerebral and spinal meninges, numerous punctate hæmorrhages in the spinal cord, and a rupture of the pleura." In another case proved by inoculations, J. Douglas found "the brain moderately congested, also the pons and medulla and especially the floor of the fourth ventricle." Tchernischeff also found small hæmorrhages in the floor of the fourth ventricle, besides intense hyperæmia of the white and gray substance of the cord, etc. Finally Anglade and Choireaux,<sup>299</sup> in a series of comparative experiments, found that intense hyperæmia appeared early and simultaneously in the blood-vessels and neuroglia (which, as I have pointed out, are neural capillaries) and that these lesions were not specific to rabies, but were observed in other disorders, including epilepsy. As to the throat and œsophagus being the seat of spasm earlier than other structures being due to the proximity of the pituitary body, Bradford<sup>300</sup> refers to the fact that "a wound of the face, inasmuch as it is near the central nervous system, is for that reason more dangerous." The *sensorium commune* of the posterior pituitary is essentially the central motor system under these conditions, as I have shown.

The primary cause of rabies is a specific virus, the nature of which has not so far been determined, introduced into the bitten tissues with the saliva of the rabid animal. The development of the disease, *i.e.*, the spasmodic period, which usually ends fatally, depends upon the antitoxic efficiency of the bitten subject's blood:—if this is adequate, as is the case in about 84 per cent. of individuals bitten by rabid animals, the virus is soon destroyed and rabies does not develop; if it is not, the virus indirectly initiates the disease.\* In the latter case the interval between the time of infection and the appearance of rabies constitutes the period of incubation, and the duration of this period is therefore proportionate with the antitoxic properties of the blood.\*

\* Author's conclusion.

<sup>296</sup> Van Gehuchten and Nélis: Presse médicale, vol. vii, p. 113, 1900.

<sup>297</sup> Babès: Wiener med. Blätter, Bd. xviii, S. 665, 1895.

<sup>298</sup> Krauss: Phila. Med. Jour., Jan. 26, 1901.

<sup>299</sup> Anglade and Choireaux: Progrès méd., May 31, 1902.

<sup>300</sup> Bradford: *Loc. cit.*

During the incubation the virus is likewise destroyed by the blood's auto-antitoxin, but only in the arteries, arterioles and capillaries that contain leucocytes, because these cells supply the proteolytic ferment and nuclein which, with oxidase, form the auto-antitoxin.\* As, conversely, adrenoxidase-laden plasma devoid of leucocytes circulates in the nervous elements, *i.e.*, the axis-cylinders, dendrites, etc., the neuroglia and neuroglia-cells and all other neural capillaries, what virus penetrates into them is not destroyed and it accumulates therein.\* Hence the fact that the virus is found in the nervous system and not in the blood.\*

The penetration of the virus into the nervous system is a normal result when, in accord with my views, all nervous elements contain plasma derived from the general circulation.

The minute quantity of virus that is capable of causing rabies, and its presence in relatively large quantities in the nervous system and some glands, and many other facts, involve the need of some organism such as the bacillus tetani that is capable of secreting toxins. Bradford<sup>301</sup> concludes a review of the evidence to this effect with the statement that although "it cannot be said that the identity of the organisms of rabies has been clearly established" . . . "there are many strong arguments in favor of the disease being of microbic origin." He regards Leblanc's statistics as to the proportion of persons bitten by rabid animals, and which place it at 16 per cent., as probably the most accurate.

Duboué<sup>302</sup> is credited by Pasteur<sup>303</sup> with the statement that the virus "propagates itself insensibly even to the central nervous system along the nervous fibers"—the first suggestion to this effect confirmed by Roux and many others. Pasteur, Burdach, Catani, Di Vestea and Zagari<sup>304</sup> and others also found that the intra-nervous inoculation was the more effective in producing the disease experimentally.

The attenuation of the virus obtained by Pasteur by inoculating monkeys in succession has not so far been explained: it is readily accounted for by the presence of auto-antitoxin—the proteolytic triad—in the blood of these animals.\* Nor has the manner in which the prophylactic effects of the Pasteur treatment are produced been shown: As I have previously pointed out,<sup>305</sup> "the extract of desiccated cord injected raises the anterior pituitary body's functions to their normal standard and sustains them until all danger is past." In other words, it stimulates the test-organ and the blood of the exposed subject is rendered sufficiently rich in antitoxin to insure the destruction of the virus. That it is upon the functional efficiency of the adrenal system, therefore, that the development of rabies depends, is obvious.

The time finally comes, however—weeks in some, months in others—when the gradual decline of catabolic activity due to

\* Author's conclusion.

<sup>301</sup> Bradford: *Loc. cit.*

<sup>302</sup> Duboué: "De la physiol. path. et du traitement rationnel de la rage," Paris, 1879.

<sup>303</sup> Pasteur: C. r. de l'Acad. de méd., Jan. 13, 1881.

<sup>304</sup> Di Vestea and Zagari: Giornale interne delle sci. mediche, vol. xi, p. 81, 1889.

<sup>305</sup> Sajous: Phila. Med. Jour., Mar. 7, 1903.



this inhibition of the adreno-thyroid mechanism by the virus, provokes so great an accumulation of toxic wastes in the blood that notwithstanding its torpor, the test-organ is caused to react.\* The adrenals and the thyroid apparatus being stimulated, the blood receives a large excess of adrenoxidase and, as a result, a corresponding surplus of trypsin and leucocytes, the source of nucleo-proteid granules.\* The thyroid apparatus being also and simultaneously activated, thyroidase accumulates in the blood along with the phagocytes produced during the leucocytosis.\* On the whole, the blood suddenly becomes laden with auto-antitoxin and germicidal cells, to destroy the virus if possible.\* If this supreme effort—which marks an advanced stage of the disease—fails,\* the paralyzing influence of the virus continues and death soon follows.

The reaction to the accumulation of these toxic wastes, in other words, is the spasmodic period of the disease, the fully developed rabies.\* This disease differs only from tetanus in that the toxæmia is more profound, and in that the virus tends, owing to its paralyzing influence on the nerve-centers, to limit the convulsions of the extremities. The paralytic phase of the disease coincides with the time when, the virus having obtained the upper hand, it paralyzes the central nervous system.\*

The true action of the virus is clearly illustrated by the so-called "paralytic" form of rabies first described by Van Swieten, in 1771. Anders<sup>300</sup> refers to this disease as follows: "In man there is a paralytic form of rabies, but it is rare as compared with the delirious or psychic type. Thirty cases have been reported by Gamaléia, and it is apt to follow deep and multiple bites. The paralysis begins near the part bitten and spreads until it becomes general, finally involving the respiratory centers." If the virus is a direct spasmogenic agent, why should the large quantities introduced fail to produce spasm? Experimental inoculation points in the same direction. In rabbits, guinea-pigs and other herbivora, the paralytic form is the prevailing one, as is well known. In rabbits, Di Vestea and Zagari observed that "from the fifth day after infection, the temperature rises with light febrile movements, to fall suddenly with the coming on of the first paralytic symptoms until the resulting death." We have in the febrile state the reaction of the adreno-thyroid center, but the convulsions witnessed in carnivora fail to appear. This obviously shows that the spasms are in reality grafted upon the true disease.

**Prophylactic Treatment.**—If an extremity is bitten, a ligature should be placed immediately above the lesion to encourage bleeding and reduce the amount of virus distributed by the

\* Author's conclusion.

<sup>300</sup> Anders: "Practice of Medicine," p. 359, 1905.

afferent vessels. The wounds and all their recesses should then be carefully cleansed and then aseptized with *hydrogen peroxide*, or a 5-per-cent. solution of *potassium permanganate*. Cauterization is of distinct value; *nitrate of silver* has been highly recommended, and pure *carbolic acid* likewise. Experiments have shown, however, that opening of the wound under anæsthesia and thorough cauterization with fuming *nitric acid* gave the best results.

Gowers<sup>307</sup> states that "it is doubtful whether the disease ever occurs if a stick of nitrate of silver is immediately plunged into a wound." Youatt<sup>308</sup> considers nitrate of silver sufficient; having obtained a failure in a single case out of 400. F. Cabot<sup>309</sup> conducted a series of comparative experiments to determine which was the best cauterizing agent, and concluded that fuming nitric acid was the most effectual substance for cauterization, and that it was of great value if employed within the first 24 hours. J. C. Vaughan<sup>310</sup> states that a couple of drops suffice in the wound made by a tooth. The slough soon separates, leaving a clean wound which heals readily.

**AGENTS WHICH INCREASE THE BACTERICIDAL AND ANTI-TOXIC PROPERTIES OF THE BLOOD.**—Pasteur's *preventive inoculations*, we have seen, owe their virtue to their stimulating influence upon the adreno-thyroid center; they enhance, therefore, the efficiency of the body's auto-protective functions.\* The earlier the treatment is begun the better; as soon as the wounds are treated as above and dressed, the patient should be sent to the nearest Pasteur Institute. The dog should not be killed, since the non-development of rabies in the animal within a few days affords proof that the bites were benign.

Pasteur Institutes have been established in New York, 313 West Twenty-third Street; Baltimore, corner of Saratoga and Calvert Streets; Chicago, 228 Dearborn Avenue.

Other prophylactic measures have been suggested. Bouchard used successfully in animals a fluid obtained by filtration from rabies-infected nerve-tissue. Babès, in collaboration with Lepp, Cerchez and Telescu,<sup>311</sup> likewise conferred immunity in animals with a serum of inoculated dogs—a result also reached by Tizzoni, in collaboration with Schwartz<sup>312</sup> and Centanni,<sup>313</sup> with sera obtained from rabbits and sheep. These agents have failed to gain the confidence of the profession. The serum recommended by Tizzoni is far more powerful than that of Babès;

\* Author's conclusion.

<sup>307</sup> Gowers: "Diseases of the Nervous System," vol. ii, second edition, p. 925, 1893.

<sup>308</sup> Cited by Tyson: "Practice of Medicine," p. 187, 1905.

<sup>309</sup> Cabot: Med. News, Mar. 18, 1899.

<sup>310</sup> J. C. Vaughan: Indian Med. Gaz., Aug., 1896.

<sup>311</sup> Babès: Ann. de l'Inst. Pasteur, vol. iii, p. 384, 1889; vol. v, p. 627, 1891; vol. viii, p. 434, 1894.

<sup>312</sup> Tizzoni: Riforma Médica, 1892.

<sup>313</sup> Centanni: All. della Reale Accad. dell. Sci. dell. Inst. di Bologna, Feb. 10, 1895.



but the fact that it is obtained from herbivora suggests the reason for this: being poor in antitoxin, the blood of these animals is rich in virus. Babès's serum obtained from Carnivora is less dangerous, the virulence of the virus being mitigated by the potent antitoxin found in the blood of such animals; but in the Pasteur method the material used at first is obtained from spinal cords in which the virus has been rendered inactive, and it is only when (from my viewpoint) the blood has thus been rendered richer in antitoxin that the virulent cords are used. It is, therefore, the least dangerous method of its kind.

P. B. Hadley<sup>314</sup> wrote recently: "Of 1608 cases treated at the New York Pasteur Institute previous to 1901, only four gave symptoms of disorders which could be traced directly to the treatment. Three had a partial paralysis of the lower limbs, lasting from one to three weeks; one patient had facial paralysis lasting four weeks. All of these cases made uneventful recoveries. The anti-rabic vaccinations may cause a slight nervousness among neurasthenic and hysterical persons; but these disturbances are never serious and are extremely rare. As to actual fatalities, records show that out of 1367 persons treated at the New York Pasteur Institute in the years 1890 to 1900 there were nine deaths, a mortality of 0.65 per cent. In 1900, from January to September, at the New York Pasteur Institute, there were 921 cases treated and two deaths, representing a mortality of 0.1 per cent. From October 1, 1904, to October 1, 1906, there were 486 treatments with one death, representing a mortality of 0.206 per cent. Reports from other institutes show about the same results; and finally, a compilation of statistics from the reports of the Pasteur Institute of Paris for the last twenty years shows that, out of 20,000 treatments, the mortality rate has been 0.25 per cent."

Unfortunately not every one can bear the direct and traveling expenses which the Pasteur treatment involves, especially in this country, where the Pasteur Institutes are few. The need of equally active prophylactic agents, offering also the advantages of being within the reach of any physician, is, therefore, very great.

When the spasmodic or second stage of rabies is allowed to develop, the patient is practically doomed, his auto-protective functions being virtually paralyzed.\* *It is upon the efficiency of the preventive measures, therefore, that his life depends.\** Both the virus and the toxic wastes being destroyed by the blood's auto-antitoxin, and *thyroid extract* causing a rapid increase of the latter, this remedy not only meets the conditions of a powerful prophylactic, but being available everywhere, its use may be begun at once; 3 grains (0.19 gm.) should be given every two hours, in adults.\* As its untoward effects are due to vasoconstriction of the cardiac coronaries, which, when excessive, inhibits the heart,\* the action of the remedy should be watched; and if the pulse become weak or dyspnoea appear, the dose should be reduced. After the second day, 5 grains (0.3 gm.) three times a day after meals suffice to sustain the

\* Author's conclusion.

<sup>314</sup> P. B. Hadley: Providence Med. Jour., Jan., 1907.

antitoxic activity of the blood above the normal standard—above, in other words, the efficiency required to destroy the virus.\*

The pathological kinship between rabies and tetanus, and the remarkable effects of thyroid extract in the tetanic convulsions that follow extirpation of the thyroid, distinctly point to this remedy as valuable in this connection. We have seen that the proportion of adrenoxidase can be gauged by the coagulation time and that thyroid extract rapidly increases the blood's coagulating properties, and that the proportion of adrenoxidase betokens a corresponding increase of antitoxin. Strychnine, we have seen, likewise enhances the formation of oxidase. Fleet-Surgeon Thorpe<sup>315</sup> recently ascertained that a remedy used successfully by the Chinese not only as a prophylactic, but as a cure in the early stages of developed cases, was a species of strychnos seed which, on analysis, gave the characteristic tests of brucine and strychnine, the former being in excess. In India, an insect closely related to the ordinary *cantharis vesicatoria* is used with success, according to Kotak.<sup>316</sup> This coincides with the Russian method, *i.e.*, hypodermic injections of potassium cantharidate,  $\frac{1}{80}$  to  $\frac{1}{20}$  grain (0.001 to 0.002 gm.), or tincture of cantharides, 10 minims (0.6 gm.) three times daily. Garlic is extensively used by the Arabs. All these agents are powerful adrenoxidase stimulants—though all much less so than thyroid extract.

Moreover, a number of observers have found that *in vitro* the blood destroyed the virus in from 15 to 22 hours; but, as previously stated, such experiments have but little value, the adrenoxidase being promptly reduced by the phosphorus-laden nucleo-proteid in the plasma.

Among other agents which powerfully stimulate the adrenal center and enhance, therefore, the production of auto-antitoxin, are the *iodides*, the *biniodide of mercury*, and *digitalis*. The first named most nearly approximates thyroid extract as a prophylactic.\* Less active as adrenal stimulants are *strychnine* and *quinine*; but by stimulating, in addition, the vasomotor and motor centers, and causing general vasoconstriction, they cause accumulation of the blood in the cutaneous capillaries, including those around the injured area, where the auto-antitoxin can best destroy the virus.\* *Cocaine* suggests itself as an efficient protective agent in this connection, but the danger of initiating the cocaine habit should be borne in mind.\*

The rapidity with which the hydrochlorate of quinine drives the blood towards the periphery and thus overcomes a localized accumulation of pathogenic organisms, their toxins and detritus, is well shown by its effect in the treatment of furuncle. Even if the boil is one of a long series, 3 grains (0.18 gm.) every three hours cause a flushed face, tinnitus, headache, etc., after eight or ten doses. When this stage is reached, the furuncle rapidly recedes. In some of my cases it began to do so after the sixth dose. This method should not be used in subjects in which arteriosclerosis is likely to be present. Smaller doses,

\* Author's conclusion.

<sup>315</sup> Thorpe: Lancet, May 14, 1904.

<sup>316</sup> Kotak: Indian Med. Record, Feb. 15, 1893.



say 2 grains (0.13 gm.) with 1 grain (0.065 gm.) of thyroid, given in the same manner, soon increase the proportion of oxidase in the blood without, in the average case, causing either tinnitus or the other phenomena mentioned. Cocaine might be used in the manner I have indicated under "Coca and Cocaine."

*Heat* is a powerful prophylactic. By exposing the bitten extremity of the body to a vapor bath until free sweating occurs, blood is not only drawn to the surface and the injured area, but the proteolytic activity of its antitoxin is greatly enhanced.\* The chances of insuring destruction of the virus are, therefore, correspondingly increased.\* Its immediate use should be supplemented by another sitting, after the blood's antitoxin will have been augmented by means of thyroid extract or one of the above-named adrenal stimulants.\*

We have seen that the proteolytic activity of ferments in auto-antitoxin is greatly increased by a marked rise of temperature. The use of the vapor-bath was recommended by Buisson, and has been used successfully in many instances. The unsatisfactory explanations given as to its physiological action, and its use by laymen, have caused the method to fall into disrepute. But Shepard<sup>317</sup> has collected a number of *bona fide* instances in which it had been used successfully by physicians not only as a preventive, but also in fully developed cases. My interpretation of its physiological action accounts for these results.

Irrespective of the Pasteur method, the foregoing measures appear to me ample to prevent the development of rabies in subjects bitten by rabid animals.

As in tetanus, the *diet* is an important feature of the morbid process.\* The fact that the spasmodic stage does not, as a rule, occur in some herbivora, points to the need of avoiding the accumulation of toxic wastes derived from animal foods, *i.e.*, of prohibiting the use of meat until all danger is past.\* The patient should also drink water freely in order to facilitate the elimination of end-products of metabolism.

**Treatment of Developed Rabies.**—In the light of my views, the measures recommended for the corresponding stage of tetanus are as applicable in rabies. The reader is therefore referred to page 1446.

If used promptly, *i.e.*, during the premonitory stage, these measures, supplemented by others described below, may turn the tide in favor of the patient. As the saliva in cases of developed rabies has been proved to be infectious, the attendants should carefully cover any abrasion that they may have on the hands or face.

\* Author's conclusion.

<sup>317</sup> Shepard: Jour. Amer. Med. Assoc., Oct. 23, 1897.

As *mercury* and *iodide* stimulate most actively the adrenal center, it is apparent that *thyroid gland* must be effective in rabies as it is in tetany, but in larger doses, since the virus tends to paralyze the test-organ.\* Either of the former agents may be used when the thyroid extract cannot be obtained.\*

Again, inasmuch as the spasmogenic agent is in rabies, as it is in tetanus, an autotoxin, the *antitetanic serum* meets the needs of the situation. It should be used in large doses, however, and injected into the median basilic vein.\* Many of the successful cases reported had been bled; but as *bleeding* alone provokes tetany by diminishing the volume of fluid in which the spasmogenic autotoxin is dissolved, it should be promptly supplemented by intravenous injections of *saline solution*.

That spontaneous cure may occur has been shown experimentally by Högyes.<sup>318</sup> Out of 159 animals in which the virus was injected in fatal doses, recovery occurred in 13 instances in which Pasteur preventive inoculations were used. The seven animals treated by the Pasteur method recovered. Laveran<sup>319</sup> and Chantemesse<sup>320</sup> have likewise reported *bona fide* cases which led them to conclude that rabies was not necessarily fatal. Although the many cases cured during the earlier portion of the nineteenth century suggest the possibility of errors in diagnosis, the fact remains that, according to Lucas Benham,<sup>321</sup> *mercury* held a prominent place in the 50 instances of recovery cited. Illingworth<sup>322</sup> recommends intramuscular injections of the biniodide of mercury with sodium iodide (1 to 50).

The use of saline solution was praised by Magendie many years ago. The reasons adduced in favor of Baccelli's *carbolic acid* treatment obtain as well in rabies, and there is reason to believe that it would prove very efficacious in this disease, since, as observed by Blasi and Travali, the virus is easily destroyed by antiseptics, especially creolin. Moreover, the oral use of a solution of carbolic acid has been highly recommended by Déclat and Peyroulx<sup>323</sup> as a prophylactic.

The *vapor-bath* has occasionally given good results even when the convulsive period was well advanced. During the premonitory stage, the procedure may be carried out readily, but when the convulsions have begun, it is sometimes necessary to fasten the patient to the bed or chair.

Interpreted from my standpoint, as previously stated, the proteolytic, *i.e.*, antitoxic, property of the blood is greatly enhanced by heat. Kellogg<sup>324</sup> states that "the effect of the vapor-bath upon the body temperature is very profound, the rectal temperature rising in the course of 20 or 30 minutes to the extent of 3 to 4 degrees." Again, "the axillary

\* Author's conclusion.

<sup>318</sup> Högyes: Orvosi Hetilap, vol. v, p. 36, 1889.

<sup>319</sup> Laveran: Semaine médicale, vol. xi, p. 180, 1891.

<sup>320</sup> Chantemesse: *Ibid.*, vol. xi, p. 180, 1891.

<sup>321</sup> Lucas Benham: Lancet, Mar. 1 to 15, 1890.

<sup>322</sup> Illingworth: "Abortive Treatment," p. 19, 1888.

<sup>323</sup> Déclat and Peyroulx: "L'acide phénique," Paris, 1874.

<sup>324</sup> Kellogg: "Rational Hydrotherapy," p. 703, 1901.



temperature rises more rapidly and to a higher point than the rectal temperature." Obviously the bath inhibits for a time the elimination of heat and thus provokes a temporary fever, which, like all febrile processes, serves to destroy the pathogenic element.\*

Buisson's own case hardly warrants the diagnosis of rabies; but instances of unmistakable rabies in which the Buisson method was successfully employed were observed by Leon Petit, Hermance, Cameron, Gray and others.<sup>325</sup> Some of these used the Turkish bath; but as Kellogg says: "The temperature of both the rectum and the axilla rises much more quickly in the vapor-bath than in the Turkish or dry hot air bath." Others apply the cold-sheet after the vapor-bath; but this imposes upon the patient an unnecessary hardship, and drives the blood into the deeper vessels, including neural capillaries. The longer blood is kept in the peripheral capillaries, the longer, of course, the virus and the spasmogenic autotoxins will be exposed to the blood's proteolytic action.

MEASURES WHICH CONTROL SPASM.—Here, again, the measures recommended for the corresponding stage of tetanus are indicated, but only when their use is necessary to arrest the spasms or reduce their violence while the blood's auto-antitoxin, augmented by either of the remedies mentioned, is counteracting the paralyzing influence of the virus.\* The latter is in reality the death-dealing agent in rabies, and to destroy it should be our aim.\* The bromides, chloral and kindred drugs being themselves paralyzants,\* *amyl nitrite* inhalations are preferable, though the former cannot be dispensed with, as a rule.

A ten-per-cent. solution of *cocaine hydrochlorate* sprayed, not into the mouth, where it is wasted owing to great amount of saliva secreted, but into the nasal cavities as far back as possible, suggests itself as a valuable adjuvant to prevent paroxysms.\* It trickles down the post-nasal cavities and the pharyngeal wall and by anæsthetizing the superficial sensory terminals of the latter, inhibits the intense reflex irritability so manifest in this region.\*

Osler<sup>326</sup> recommends the local application of cocaine, but the quantity of saliva in the mouth and the irritability of the pharynx render this measure very difficult. Free spraying into the nose while the patient is in the recumbent position is readily accomplished.

\* Author's conclusion.

<sup>325</sup> Cited by Shepard: *Loc. cit.*

<sup>326</sup> Osler: "Practice of Medicine," third edition, p. 229, 1898.

## CHAPTER XXV.

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

## PAIN-CAUSING DISORDERS DUE TO HYPOACTIVITY OF THE ADRENAL SYSTEM.

Balfour<sup>1</sup> wrote a few years ago, referring to the pathogenesis of gout: "With all our increased accuracy in details, it does not appear that our ideas of what gout really is are any clearer or any better defined than those of our forefathers." If anything, the obscurity surrounding this question may be said to have become greater, more recent investigations having overthrown those which ten years ago seemed of great promise. Even these modern products of the laboratory evidently rest upon a very weak foundation, for Graham Lusk in a recently published work<sup>2</sup> (1906), closes a review of purin metabolism in gout with the suggestive remark that "present-day doctrines concerning metabolism in gout may shortly become entirely obsolete through new and far-reaching discoveries." In truth, the labor that physiological chemists have devoted to this subject, though fruitful as to valuable experimental facts, has remained sterile as to final results, and will continue to do so because they persist in ignoring the cardinal functions of the adrenal secretions in metabolism and in the life process itself, where their work has proven as futile. Indeed, Lusk also writes<sup>3</sup> in this connection: "However clearly formulated the laws of metabolism may be, and many of them are as fixed and definite as are any laws of physics and chemistry, still the primary cause of metabolism remains a hidden secret of the living bioplasm." It is only by a broad and generous conception of all available lines of knowledge that we can ever hope to solve these great problems which, as we have already seen, involve several of the scourges of mankind.

<sup>1</sup> Balfour: *Edinburgh Med. Jour.*, June, 1898.

<sup>2</sup> Graham Lusk: "The Elements of the Science of Nutrition," p. 287, 1906.

<sup>3</sup> Graham Lusk: *Ibid.*, p. 297.