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The Pathology of the Cranial Nerves in Tabes Dorsalis.

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THE PATHOLOGY OF THE CRANIAL NERVES IN TABES DORSALIS.[1]

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Symptoms referable to the oculomotor and especially to the abducens nerves are very frequent and often precocious in tabes dorsalis, and it is strange that the anatomical changes underlying these have so long escaped detection. The transitoriness of many cases of diplopia occurring in tabes has been believed to account for this, but this argument is invalid in cases in which the strabismus is permanent, and such cases are not infrequent. The cause of the Argyll-Robertson pupil has been a constant puzzle to neurologists, and it still remains so, as we are not yet sufficiently informed of the course of the fibers subserving the reaction of the pupil to light. This paper will not solve that riddle, although the facts herein presented may afford a substratum for future research concerning iridoplegia in tabes. Regarding oculomotor paralysis, at least, the facts here presented demonstrate the morbid anatomy and appear to solve the pathogenesis. Read in conjunction with preceding articles,[2] they very fully show the etiology, mode of genesis, and microscopic appearances of the cranial nerve palsies occurring in tabetics and paretics, both at their inception and after the disability has become permanent. The facts add one more stone to the edifice of the luetic origin of taboparesis, and afford another illustration of the explanation offered by Nageotte[3] as to the pathogenesis of those disorders.

The Initial Lesion of Tabes. It will be remembered that as long ago as 1894[4] the French neurologist presented preparations

[1] Through the kindness and courtesy of Dr. Clovis Vincent, of Paris, I have been enabled in this article and in a preceding one (*New York Medical Record*, January 29, 1910) to place before American readers the main data of the two sets of investigations which Dr. Vincent has been pursuing during the last five years in the clinics of the Parisian hospitals, La Pitié, La Salpêtrière, and St. Louis, and in the laboratories of Babinski and Nageotte, Raymond, and Chauffard. The reader will see that the results of Dr. Vincent's researches afford still further corroboration of the ideas so long upheld by Babinski and Nageotte, that all the symptoms of taboparesis ensue upon a chronic meningitis of syphilitic nature. The data here expounded clearly show the untenability of the dystrophic theory of taboparesis.

[2] Medical Record, January 29, 1910; Amer. Jour. Med. Sci., August, 1908.

[3] La Pathogénie du Tabes Dorsalis, Paris, 1904.

[4] La Pathogénie du Tabes Dorsalis, Paris, 1904.; Soc. Méd. des Hôp., 1894.

showing that the initial lesion of tabes dorsalis consists of a chronic inflammation of the posterior and often the anterior spinal roots—a transverse radiculitis. He showed that the seat of election of this process is the situation where the anterior and posterior spinal roots, in approaching one another, are surrounded by the funnel-shaped prolongation of the meninges which cover them before being pierced by them at their exit from the theca vertebralis. The gradual approximation of the meninges at this spot, he believed, produced a concentration of toxic or inflammatory materials around the nerve fibers traversing what he called the radicular zone. An arachnoiditis became a perineuritis, and finally spread into an endoneuritis. It was to this process that was due the degeneration of the posterior columns of the spinal cord. Although the anterior roots participated, their power of regeneration frequently prevented permanent paralysis and muscular atrophy; but perhaps 20 per cent. of tabetics did show some muscular atrophy sooner or later.

As a preliminary to what is to follow, no more than this need be said, for Nageotte's preparations are figured and the evidence presented in some detail in a previous article;[5] and in a shortly forthcoming communication[6] the further questions are taken up regarding the recent biochemical hypotheses which Mott[7] has advanced to reconcile the syphilitic etiology of tabes with the dystrophic theory so long held by the majority of English and German neurologists.

Reflex Iridoplegia and the Sympathetic Nerve. Future research as to the pathogenesis of the Argyll-Robertson pupil, that long-standing puzzle of neurologists, may find its direction in the lines of this investigation, for it will be noted in Vincent's case that there was no examination of the sympathetic fibers in and around the cavernous sinus, for, of course, the almost complete ophthalmoplegia could itself account for the iridoplegia of this patient. But if studies of this kind fail to reveal, in cases showing the Argyll-Robertson pupil, any lesions of the third nerve and lenticular nucleus, the incrimination of the sympathetic might be probable, for Roux[8] has shown how, in the spinal region, the sympathetic fibers are very often attacked in tabetics en route from the cord to the ganglionated chain, and that they are attacked as they traverse the radicular zone of Nageotte along with the sensory or motor fibers of the cerebrospinal system.

The mechanism of the light reflex is not yet decided. It has been considered a simple sensorimotor one, and its mechanism sought for along the arc, afferent optic fibers, synapse neurone, efferent third nerve fibers, for it is abolished by destruction of any of these. But we are by no means certain that it may not be an inhibitory phenomenon due to an arrest by the stimulus of light of the dilatatory im-

[5] Amer. Jour. Med. Sci., August, 1908; also Brit. Med. Jour., October, 1909.
[6] International Clinics, Spring, 1910.
[7] Brit. Med. Jour., 1909, i.
[8] Thèse de Paris, 1900.

pulses of some part of the ciliospinal or other mechanism travelling by the cranial sympathetic. In that case we should interpret the light reaction as due to a withdrawal of the antagonizing tonus of the dilator iridis from the balancing tonus of sphincter iridis, whereby the latter prevails and produces pupillary contraction; but it can do so, of course, only when its fibers in the third nerve are intact and when an afferent stimulus is possible. But if at the state of rest the sphincter tonus is unopposed from paralysis of the dilator, of course contracture of the pupil remains constant, because unopposed, and naturally the dilator afflux, already removed by disease, will not be influenced by light. In other words, an Argyll-Robertson pupil would be one that does not dilate in the absence of light.

Some tabetics' pupils are fixed in dilatation, which, on the theory now promulgated, would be explained by interference with the third nerve afflux by meningitic processes, thus leaving the dilator tonus in full sway; though it is hard to explain why such pupils do not further dilate in the absence of light (if, indeed, they do not), and thus give the appearance of contracting to the stimulus of light. At all events, it is hardly likely that a meningeal inflammation so widespread as that which causes tabes could fail to implicate some of the sympathetic fibers in their course in the cranial cavity. The difficulties of the research should be obvious, but in these days of serial sections they should not be insurmountable. It is possible, too, that the sympathetic contains sphincter fibers also, for Jegorow[9] states that he found greater dilatation of the pupil after excision of the ciliary ganglion than he did after proximal cutting of the third nerve; and François-Franck,[10] too, found that cutting the ciliary nerves caused greater dilatation than did cutting the third nerve.

The Case. In the case now to be described,[11] a meningitis of long standing, no longer in activity, had left its traces merely in hyperplasia of the connective tissue of the nerve and partial destruction of the noble elements. The patient was a woman, aged fifty-one years, married at eighteen, with five healthy children and two miscarriages, the last in 1885, accompanied by sore throat and followed by an attack of headache, delirium, convulsions, and coma. It was most probably a meningitis, for she remained quite blind, and had frequent attacks of focal epilepsy on the left side.[12] In 1891 Gombault had found psoriasis, blindness, laryngeal trouble, and focal epilepsy, the last disappearing. On admission the nutrition was good. There was a syphilitic perforation of the palate. There was gray atrophy of the optic papillæ, with contraction of the vessels. Even light was unperceived. There was partial ptosis, especially of the left lid. Ocular convergence was impossible. Internal

[9] Arch. Schlav. de biol., Paris, 1887, tome iii, 332.
[10] Trav. du lab. de Marey, 1880, tome iv.
[11] See Vincent, Thèse de Paris, 1910.
[12] See Souques, Soc. de neurol., May, 1905.

lateral movements could not be accomplished, nor could the raising or lowering of the globes; but the external movements could be performed. The left pupil was larger than the right. There was no reaction to light, and that on attempting convergence and distant regard was defective. The sensibility of the cornea and the reflex lacrymal secretion were present. Bilateral nystagmoid movements occurred.

Thus, there was complete paralysis of all the acts governed by the third nerve, with the exception of the pupillary reaction upon accommodation, convergence, and distance. Respiration was more rapid than normal—28 per minute. It was interrupted by paroxysms, especially after excitement. During these, breathlessness and angoisse appeared, a "whooping" cough distressed her, the face reddened, and there was often abundant secretion of tears and saliva.

Phonation was rough, bitonal, nasal, and often almost inaudible. The right vocal cord was paralyzed, and the right side of the tongue was atrophied, corrugated, and showed fibrillary twitchings. There was, perhaps, a little facial asymmetry. There were no basal crises nor bulbar trouble other than the foregoing. However, it was a typical case of basal tabes as regards the cranial symptoms.

There were no tabetic symptoms in the lower limbs, but the deep reflexes were exaggerated, and the toes sometimes extended when stroking the sole. There were occasional lightning pains, but no visceral incontinences, and no other trouble of the nervous functions. Lumbar puncture showed an intense lymphocytosis. The diagnosis was clearly basilar meningitis, superior tabes.

During the two years which elapsed before her death few new symptoms appeared. The Jacksonian epilepsy reappeared. It was probably due to an area of cerebral softening found post mortem in the right hemisphere. The ocular palsies improved, although she never succeeded in convergence or holding the eye for more than an instant toward the inner canthus. The atrophy of the tongue, however, persisted.

At the *autopsy* the meninges did not appear diseased, and the cranial nerves seemed unaltered in volume, except the optic nerve, which had shrunken to about the size of a normal oculomotor. The right angular gyrus showed an old softening about the size of a quarter. Under the microscope the spinal cord revealed no degeneration of the posterior roots nor of the posterior columns, where the internal bandalette was quite intact. The anterior roots were also normal.

The optic nerve showed characteristic tabetic atrophy, not a single nerve fiber being preserved. The connective tissue presented a very severe endoneuritis and perineuritis, with arteritis of the type described by Marie and Leri,[13] and due to transverse "radiculitis"

[13] Rev. neurol., 1906.

(the optic nerve is not a homologue of a spinal root); there was no lesion of the brain or eye to account for it.

Oculomotor Nerves. The lesions (Fig. 1) were nearly identical on the two sides. That of the left shows, 4 mm. after entering the parietes of the cavernous sinus (Figs. 2 and 3), a distinct focus of transverse radicular neuritis. This is shown by the hypertrophy of the nerve (Figs. 4 and 5), but above all by the presence in its interior of vast bands of fibrous tissue, which dissociated and left only a few intact fasciculi (Figs. 6 and 7). Farther down it is not so intense, and it has disappeared 5.5 mm. after the entry of the nerve into the sinus. Thus, its length is only 1.5 mm. It corresponds to the spot just behind the place where the nerve is divided into compartments by the layer of connective tissue which accompanies its anastomotic branches.

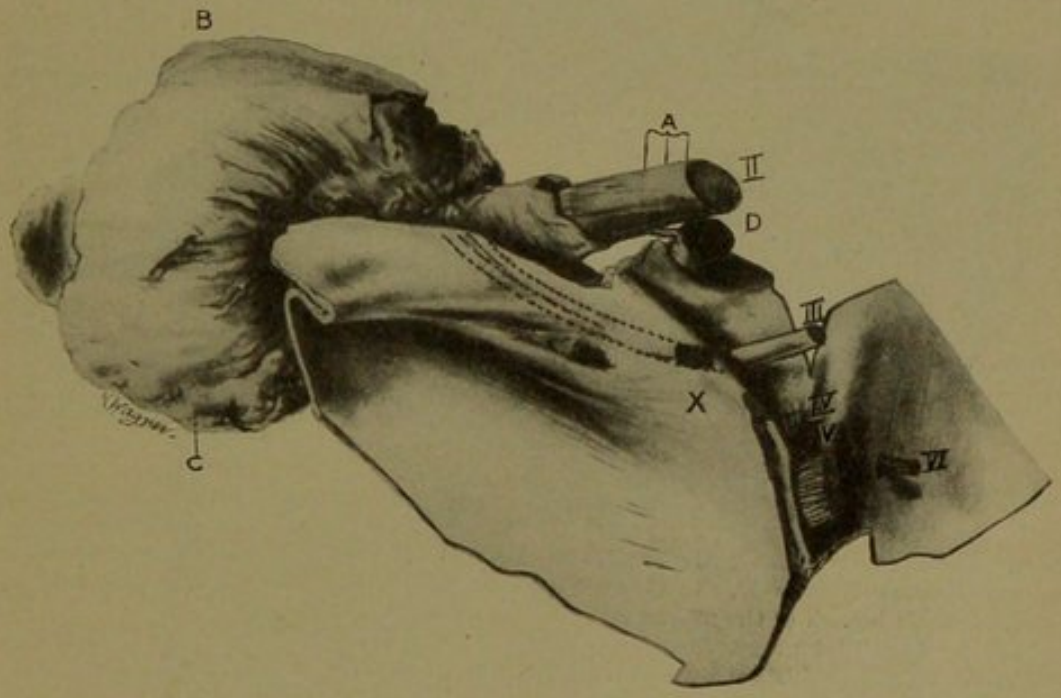

FIG. 1.—Meninges, globe of the eye, and cranial nerves removed intact to prevent tearing of the meningeal sheaths from the oculomotor nerve. The position and extent of the lesion is shown by the shaded area of the letter *X*. The subdural course of the oculomotor nerve is indicated by the dotted lines. *A*, three lines showing the direction in which the sections were made; *B*, globe of the eye; *C*, periocular fat concealing the nerves and muscles; *D*, internal carotid artery; *II*, optic nerve; *III*, oculomotor nerve; *IV*, pathetic nerve; *V*, trigeminal root; *VI*, abducens nerve.

At the parting the normal nerve becomes divided into compartments by the connective tissue, which, in a few millimeters, disappears. This is the spot where the endoneuritis has occurred. A little higher up one sees the line of the subarachnoid inflammation, now absorbed. The thickened vessel and the tucks of fibrous tissue indicate this. That the inflammatory process has not quite subsided is shown with hematein-eosin-orange stain (see original memoir). This shows that the nerve is still crammed with nuclei, and that the

neighboring meninges are much altered, even obliterated, endoneuritis appearing, and that the inflammation is still present outside

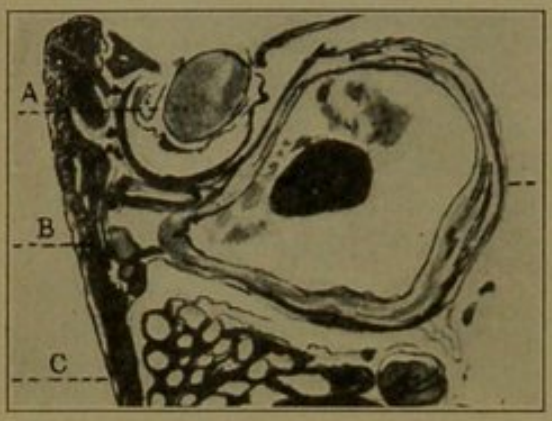

FIG. 2

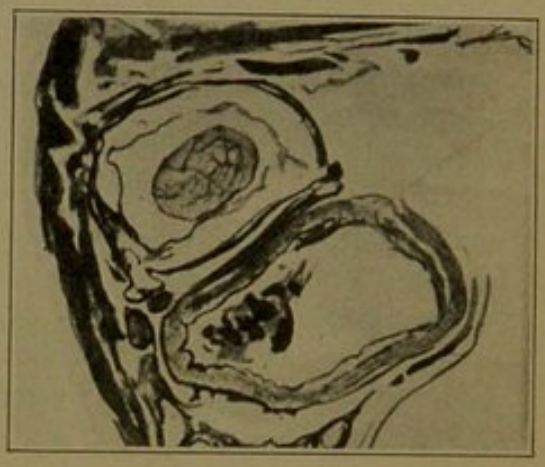

FIG. 3

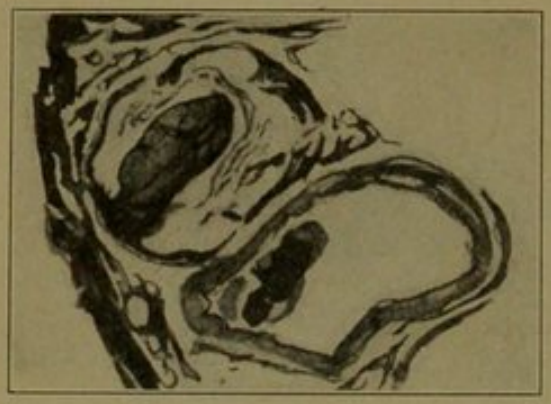

FIG. 4

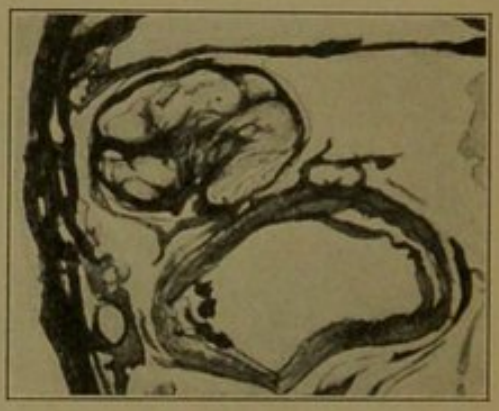

FIG. 5

FIG. 2.—Transverse section (diagrammatic) of the region shown in Fig. 1, the section being made through the cavernous sinus proximal to the mark *X*. It shows the oculomotor nerve, *A*, lying in its meningeal gutter in the root of the sinus. There is at this situation no visible arachnoiditis. *B*, situation of the fourth and sixth cranial nerves; *C*, situation of the ophthalmic branch of the fifth nerve; *D*, internal carotid artery.

FIG. 3.—The third nerve. *A*, is now completely surrounded by its canal of dura and arachnoid matter, which are not yet adherent. The trabeculæ of endoneuritis are visible; other structures are as in Fig. 2.

FIG. 4.—The inflamed arachnoid is shown adhering to the third nerve at one place. The endoneuritis is still more evident than in Fig. 3. Note the increase in volume of the nerve.

FIG. 5.—The third nerve is shown transversed and disassociated by thick trabeculæ of connective tissue. Note the enormous increase in diameter of the nerve as against Figs. 2, 3, and 4, which are drawn to the same scale. The increased volume is due to the fibrinoplastic exudate and the round-cell infiltration within the sheath.

the sheath of the nerve, with the characteristic lymphocytes and, above all, plasma cells with the perinuclear halo. Thus it is clear that we have over both third nerves the cicatrix of an old inflammatory focus of localized interstitial neuritis.

The Nerve Fibers (Figs. 8 and 9). The Weigert method shows the paleness of some of the nerve fibers among the dark violet of those remaining normal. Osmic acid shows the dwarfed and pale

fibers, as in the preceding case,[14] but, above all, it reveals islands of regeneration. Both above and below the site of the lesion these islands are quite abundant, so that under low power the nerve might be thought normal; but a higher power shows that the fibers they contain are often very small, squeezed together, without any

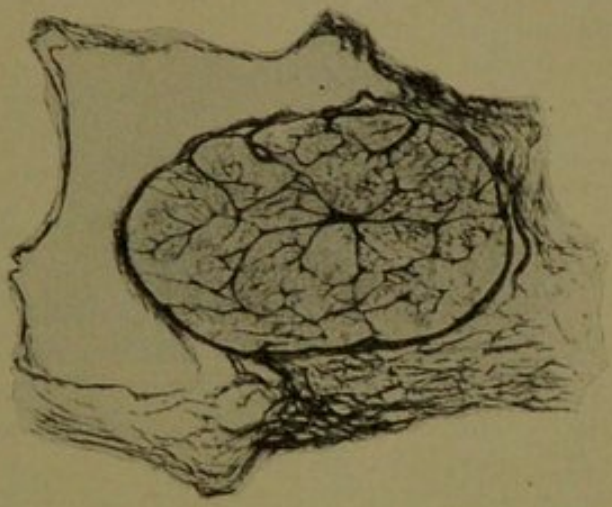

FIG. 6.—A microscopic view of Fig. 3, a transverse section of the oculomotor nerve near the commencement of the lesion. Note the endoneural trabeculæ of connective tissue and that only half the surrounding arachnoid is adherent. (Van Giesen stain.)

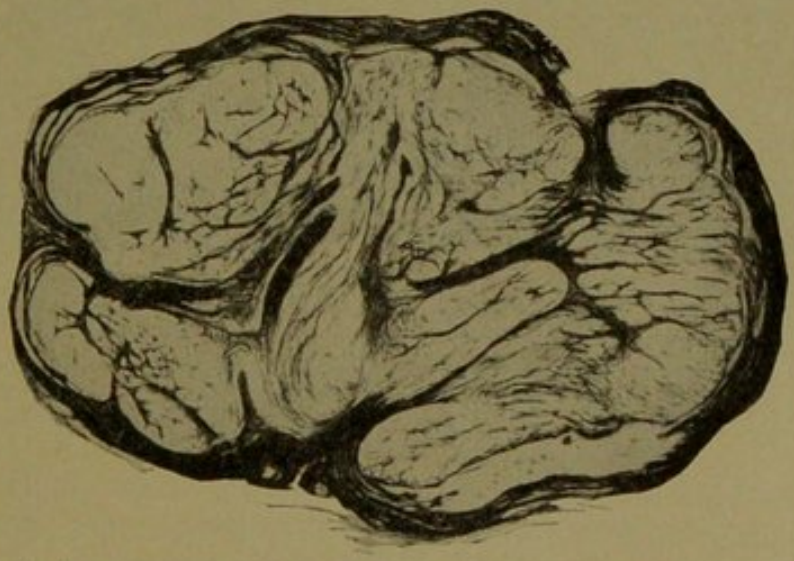

FIG. 7.—A microscopic view of Fig. 5, showing enormous neoformative endoneuritis, causing great enlargement of the nerve.

connective tissue intervening. Serial sections show that they have come from a single nerve fiber, which buds out and follows an old neurilemma tract. They are significant of the presence of a noxa in some part of the course of the nerve, and they explain the manner in which certain tabetic palsies so much improve. In this case they

[14] Med. Record, January 29, 1910.

are seen throughout the whole of the periphery of the nerve, especially in the fine branches penetrating the muscles, where their separation of the branches renders their study easier.

The hypoglossal nerve of this case shows changes in the nerve fiber similar to those of a previous case,[15] and to those of the third, in that its nucleus was untouched. It is this which accounts for the

Fig. 9

Fig. 8

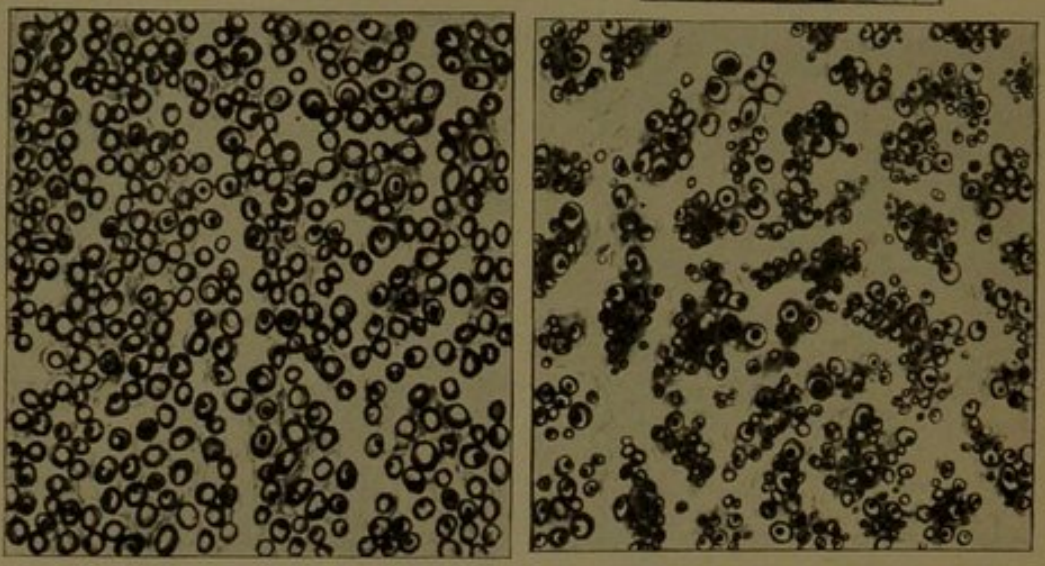

Fig. 8.—Transverse section of a normal oculomotor nerve. Note that the myelin rings and axis cylinders do not differ markedly in calibre.

Fig. 9.—The oculomotor nerve of the case studied (Azoulay method). Note the numerous atrophied fibres, small and pale, and their separation into groups by a prolilerating endoneuritis. Some regenerating fibres are seen. (Low and high power magnification.)

absence of muscular atrophy in these cases. The nuclei of none of the cranial nerves showed any alteration, although carefully studied in serial sections; so that we may conclude that in this a focus of interstitial neuritis was the cause of the tabetic symptoms.

Although even this intense lesion had not completely destroyed the functional efficiency of the nerve fibers, except the optic ones, yet it is conceivable that such destruction may, and indeed must, occur, as is shown by the lingual hemiatrophy of this case, and the fascicular palsy and reactions of degeneration of the muscle found in tabetics in varying proportions.

[15] Loc. cit.

Pathology of Fugitive Pareses. Now, although this case does not explain the genesis of the Argyll-Robertson pupil, it does furnish the missing link in the chain of evidence required to explain the fugitive palsies of the ocular muscles which so often occur in the course of tabes. For, though in this case the palsies were persistent, another series of facts makes it clear why they are not so in all cases. For example, Vincent[16] examined another case of tabes with only mild cranial nerve symptoms in which, unfortunately, the oculomotor nerves were spoiled at the postmortem, but in which the hypoglossal, which is also an anterior root homologue, showed the commencement of changes as a result of the progress of which the appearances in our present case ensue. Although no clinical symptoms had appeared, in spite of a considerable endoneuritis and loss of quite a large number of fibers in the hypoglossal, yet this is easily accounted for by the wide distribution among the tongue muscles of each fasciculus of the twelfth nerve, so that each part of the tongue has retained at least some muscle fibers, of which the innervation persists, to enable the tongue to perform its movements without apparent impairment.

Very different is the result when only a few nerve fibers supplying an oculomotor nerve are attacked. A very slight diminution of the innervation conveyed, for example, by the sixth nerve to the abducens muscle interferes with the delicate muscle balance needed for the adjustment of the optic axes in binocular vision. Hence the derangement is at once manifested clinically as a paralytic diplopia. The thinness of the abducens nerve makes it particularly liable to implication in the inflammatory process of the leptomeninges as it traverses its long course at the base of the brain.

Why, then, does the paralysis usually clear up in a few days, unlike the present case?

The Pareses of Secondary Syphilis. This question is answered by another series of facts, more especially conspicuous in what has been called the secondary stage of syphilitic affection. It is now known that even in this stage the meninges are inflamed quite often;[17] Buttino[18] believes in 40 per cent. of cases.

In addition to the general symptoms, such as headache, exaggerated reflexes, hyperirritability, and sometimes even Kernig's sign, quite a number of cases exhibit focal symptoms, such as facial paresis, local vasomotor changes, and neuralgias.[19] It is the rule for these to clear up along with the meningism, sometimes even without treatment. This only conforms to the tendency of the processes of lues venerea to resolve like those of other infective diseases.

The Continuity with the Tertiary Stage. It has been supposed that the tertiary lesions differ in this respect, but it

[16] Loc. cit.
[17] Ravaut, Méd.Soc. des Hôp. de Paris, 1901, etc.
[18] Riv. di Pat. Nerv. e. Ment., 1906.
[19] Drouet, Thèse de Paris, 1904.

is becoming evident that no distinction of kind really exists between the periods of syphilis; for, on the one hand, some cases pass to rapid paralysis and death within a few months,[20] while others show spontaneous recrudescence of symptoms[21] even many years after infection. Furthermore, Vincent's[22] examination of the cerebrospinal fluid of apparently healthy individuals having had syphilis has revealed, in several cases, an abundant lymphocytosis, and in some of these cases symptoms of tertiary syphilis of the nervous system showed themselves some months after his examination. It is clear, then, that between the secondary and tertiary stages of syphilis there is no absolute pathological or clinical differentium, as regards the nervous system at least; in either stage the lesions may be absorbed, and the structures involved may resume their function if they are not destroyed by the inflammation of the arachnoid, which is the fundamental lesion of tabes dorsalis.

Why Return of Functional Capacity Differs in Motor and Sensory Losses of Tabetics. As regards the fibers emanating from the spinal and cranial ganglia, a destruction is definitive, for the secondarily degenerated fibers within the central nervous system cannot reintegrate, nor are the regenerated fibers within the roots capable of utilizing the anlage of a former course; hence sensory losses of tabetics persist in spite of resolution of lesions.

The Role of Exercises. The return of functional capacity acquired by what is known as the Fraenkel exercises is not due to the reëstablishment of old nerve paths, or the establishment of new channels of afferent information, as is so often supposed; but it is due to the patient learning volitionally to utilize the imperfect afferent information, which is all that remains to him, and to create from it a new set of automatisms to replace those which now functionate in so disorderly a fashion as to create ataxia. But when resolution occurs in the inflammatory focus surrounding peripheral efferent fibers, the functional efficiency of the diseased nerves may be resumed, even though destruction of the nerve fibers has been complete. The reason is that the degeneration of an efferent neuron attacked while traversing the meninges is entirely peripheral; and, as we know, peripheral neurons can regenerate completely and resume their accustomed path as long as there is no mechanical interruption in the course of the growing fiber. A granulomatous cicatrix sometimes furnishes this obstacle, and then the loss of function is permanent, as in the present case.

Other Causes of Neural Syphilis, not Tabetic Intoxicative. As regards the genesis in anterior radiculitis of the muscular atrophies of tabetics, some recent pathological examinations have

[20] See case of Sicard et Roussy (Rev. de neur., 1904), in which death occurred from acute meningitis seven months after the chancre, and post mortem intense subarachnoid infiltration, periarteritis, and endarteritis obliterans were found.

[21] Ballet and Barb., Rev. neur., 1908.

[22] See author's article in Med. Rec., January 29, 1910., and Vincent, loc. cit.

been used as arguments against the conceptions here presented, and in support of the dystrophic explanation of tabes dorsalis. Such, for example, are the cases of polyomyelitis antérieur chronique in syphilitics of Pierre Marie, Jr.,[23] and of S. A. K. Wilson,[24] which their authors attribute to a slow intoxication of the neurons, for, in Wilson's cases, he did not believe that the vascular changes were sufficient to account for the destruction of the anterior horn cells which he found. Leri's[25] observations on the same disease showed how often syphilis had been an antecedent; but, when it is remembered that there was a meningitis in all of Nageotte's cases, and that there was no disease of the gray matter in them, it is not difficult to see that Marie and Wilson are dealing with quite a different condition, which, though a chronic syphilitic one, may be of the same kind as the more acute and grave syphilitic intoxications revealed by the cases of Preobraschensky,[26] in which death rapidly ensued, and post mortem no scleroses nor degeneration was found, but merely atrophy of the anterior horn and roots near the cord, along with infiltration of the vessels.

The case of Crouzon and Villaret,[27] too, was believed to be intoxicative, as, after some months of meningomyelitic sciatica, an acutely ingravescent ascending paralysis caused death in eight days in a man of forty-two. Again, in an ape, which died seven months after inoculation with Treponema pallidum, having been blind and ataxic for a month, Schroeder[28] found, post mortem, no round-cell infiltration, although the myelin of the optic nerve was entirely replaced by granules, and there was intense degeneration of the posterior columns. The ape's pupils had not ceased to react to light, and the tendon jerks had been exaggerated; Schroeder did not regard it as a case of true tabes, but of an acute intoxication. The role of the syphilitic vascular diseases in producing sclerosis of the spinal cord must not be forgotten either. Tabetics are no more immune to vascular disease of the spinal cord than other syphilitics. This is only in harmony with the frequency with which tabes and aortic disease occur together, as Babinski[29] pointed out long ago.

Vascular Changes. But there is another factor in the production of the sclerosis of the cord sometimes found in tabetics in addition to the pseudosclerosed appearance of the posterior columns produced by the secondary degeneration ensuing upon radiculitis. I refer to the perivascular infiltrations in the septa, extending into the cord from the inflamed pia mater, which have been described by Bently,[30] Paviot,[31] and Schroeder.[32] The latter found them in the brain stem

[23] Rev. neurol., 1909.
[24] Review of Neurology and Psychiatry, 1909.
[25] Rev. neurol., 1907.
[26] Neurol. Centralbl., 1908.
[27] Review of Neurology and Psychiatry, 1908.
[28] Arch. f. Psych., 1908.
[29] Rev. neurol.
[30] See Beutler, Thèse de Lyon, 06.
[31] Soc. de Méd. des Hôp. de Lyon, 1905.
[32] Centralbl. f. Nervenkrankheiten u. Psychiat, 1907.

and optic nerve as well, though not in the cortex of the five cases he examined and they did not occur in alcoholic pseudotabes. It is the same trabecular infiltration which is found in the cortex of paretics (Alzheimer[33]), but in tabes it is relatively rare, even though the pia is always thickened (Spiller[34]).

I have thought it right to mention these exceptional cases, so that the main issue should not be confused by a consideration of cases complicated by lesions of which the genesis differs so markedly from those of true tabes dorsalis. In this way the uninformed will not be deceived by criticisms of the radicular genesis of tabes; for they will know that criticisms of the nature indicated are founded upon epiphenomena which may occur in any syphilitic; although they could not be adduced with regard to the case here cited, yet they might be so adduced regarding some future case in which the cranial nerve paralysis of a tabetic was due to toxemia, arteritis, or nuclear disease. This would not be a cranial nerve tabes, for that disease, like the spinal tabes itself, is always due to the transverse radiculitis of Nageotte, whether this affects the sensory or the motor roots.

[33] Ein Beitrag zur Histopath. d. Tabes Dorsalis, 1905, etc.
[34] Philadelphia Neurological Society, 1908.