moderate dose of bromide of potassium bring out the unsightly and irritating eruption of acne which is one of its most unpleasant physiological effects. The great advantage of sulphonal is that it may be continued for prolonged periods without increasing the dose. The late Sir Henry Thompson at one time took a nightly draught, which had to be very carefully prepared because of its insoluble nature; and an active and energetic friend of mine, and one of the best shots in Aberdeenshire, has taken 10 grains three times a week for many years with good effect, and has never found it necessary to go beyond that quantity; on the other hand, it is not quite free from danger, and not very long ago an elderly lady friend of mine died from evident accumulation in her system from a series of not very heavy doses taken for purely narcotic purposes.

So much for the choice of narcotics; may I say a few words about the anatomical or pathological conditions which may interfere with their action? Sleep being produced by anaemia of the brain, what is the effect of the rigidity of the arterial system in advancing years, and which, of course, prevents the rapid variation of the conditions of circulation within the cerebral mass? and what is the precise effect of pregnancy, or alcoholism, or diabetes, or glycosuria, or Bright's disease, or blood and urine loaded with uric acid, or a congested liver, or blocking of what old-fashioned writers used to call the "primae viae" by chronic constipation? Space forbids me to pursue this suggestive line further, but if the Collective Investigation Committee of the British Medical Association, which formerly did excellent work, still exists, I would recommend this subject to their earnest consideration. For, so far as I know, either there is no sufficient information to guide us or it is so scattered as to be of comparatively little use; and further contributions to our knowledge will be gratefully received and acknowledged by those who, like myself, are ignorant, perhaps through no fault of our own.

REFERENCE.

¹ Watson, *Principles and Practice of Physic*, vol. i, p. 842.

The Morison Lectures

ON THE

PATHOLOGY OF SYPHILIS OF THE NERVOUS SYSTEM IN THE LIGHT OF MODERN RESEARCH.

DELIVERED AT THE ROYAL COLLEGE OF PHYSICIANS, EDINBURGH, JAN. 25TH, 27TH, AND 29TH, 1909.

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LECTURE III.

I ENDEAVOURED in my last lectures to indicate some of the advances made in our knowledge of the biology and bio-chemistry of syphilis, and in this my last lecture I will try to correlate the facts with clinico-anatomical knowledge, especially in relation to the etiology of the parasyphilitic affections, tabes, and general paralysis.

PARASYPHILIS (FOURNIER); METASYPHILIS (MOEBIUS).

Parasyphilis is the term given by Fournier to those diseases of which syphilis is essentially the cause, but which are not directly the result of the syphilitic virus. Such diseases are: General paralysis, tabes dorsalis, tabo-paralysis, and primary optic atrophy. These diseases are really a single morbid entity owning the same cause; insidious in onset, progressive in character, and uninfluenced by antisiphilitic remedies. These various clinical types of parasyphilitic disease are the result of a primary neuronc dystrophy; they have a similar pathogenesis, and may occur simultaneously or successively in the same individual. In tabes dorsalis the spinal sensory protoneurons are affected; in general paralysis the cortical association neurons; in tabo-paralysis both are affected simultaneously or successively. The dystrophic process is due to a lack of durability of the neurons; it may be a slow process of decay and death of the intraspinal portion

of the sensory protoneurons, as in the case of tabes dorsalis; it may be a rapid process of decay and death of systems and communities of neurons of the brain, as in general paralysis. The former is a smouldering destruction of neural elements, the latter a conflagration often fanned into flames by microbial toxæmia, autotoxæmia, or circulatory disturbances associated with arterial anaemia and venous congestion with blood stasis of the brain. It is probable that Erb's spinal paralysis and certain cases of amyotrophic lateral sclerosis may be primary post-syphilitic dystrophies.

Fournier thus classifies parasyphilitic affections:

I. ACQUIRED SYPHILIS.

1. Acute hystero-neurasthenia of the secondary period.
2. Different neurasthenic manifestations of a more advanced stage.
3. Tabes.
4. General paralysis.
5. A special form of epilepsy.
6. A special form of muscular atrophy.

II. HEREDO-SYPHILIS.

Numerous dystrophic troubles, general or partial; malformation, notably dental; arrest or retardation of physical and intellectual development, infantilism, dwarfism, inborn lack of vitality, cachexia, marasmus, rickets, hydrocephalus, certain forms of simple meningitis in early life, possibly certain cases of true epilepsy, juvenile tabes, spinal and optic juvenile general paresis. The gravity of these affections lies in the fact that they are uninfluenced by antisiphilitic treatment. The local and general failure of development may be due (1) to the direct influence of the virus upon the life and growth of the tissues, or (2) indirectly to exhaustion of the specific energy of the cells of the central nervous system by the establishment of an altered metabolism, the bio-chemical nature of which is not yet fully understood. But, as a provisional hypothesis, we might suggest that the unloosening of lipid substances into the blood, which we know occurs in congenital syphilis, may lead to a defective *vita propria* of all the cells of the body. In some lesions of congenital syphilis it may be actually due to the local invasions and multiplication of the spirochaete, for they have been found in abundance in situations where local lesions exist—for example, the epiphysis of bone—and why not in the epiblastic enamel germs?

We might provisionally suggest as a hypothesis that in all cases of acquired and congenital syphilis the living contagium, spirochaete, excites the tissues and fluids of the body to a defensive reaction. The difference in the effects of inoculation may depend upon the virus itself. Some striking examples will be given later on which apparently indicate that there may be a special neurotoxic virus, and if such instances were more numerous we could hardly believe that coincidence could explain the facts. If, as there is reason to believe, the *Spirochaeta pallida* is the living contagium, and that, becoming generalized in the lymph and blood stream, it produces the secondary manifestations, then there is a certain amount of chance what tissues will be attacked; for the living agent, swept along in the blood stream, may become lodged anywhere, and, by blocking capillaries, cause a local focus of tissue infection. The existence of a generalized eruption implies virulence of the circulating blood, and experiments demonstrate the fact that the blood is virulent during the eruptive stage; thus, Neisser has obtained a positive result by injection of blood into the skin in the chimpanzee, and Roux and Metchnikoff have successfully inoculated a macaque monkey from the blood of the chimpanzee in the eruptive period. It would be of great interest to know how long the virulence of the blood persists after the generalized eruption, or if the consecutive attacks which may occur even after fifteen or twenty years are explained by the "contagium vivum" remaining latent in the lymphatic glands or some deep-seated organ. What is the evidence in favour of this view?

It is generally admitted that the subjects of tabes and general paralysis are recruited especially from those individuals who have had a mild attack and who very seldom show any signs or symptoms of tertiary gummatous skin, visceral or bone lesions. Fournier states: "The comparative mildness of the primary constitutional symptoms in those who ulti-

mately become tabetic would almost seem to indicate that, when the syphilitic virus expends itself in severe primary and secondary manifestations, there is a less tendency to the subtle poison which proves so disastrous to the nervous system." From an experience of over 500 necropsies made on paralytic patients I have been surprised at the rarity of severe tertiary skin and visceral lesions as compared with the cases of true syphilitic brain disease. Arterio-sclerosis, in the form of fibrotic plaques of the aorta, is, however, very common in paralytic dementia, which, however, is now regarded as a parasymphilitic affection. Again, although paralytics in the prodromal stages of the disease often give themselves up to debauchery and sexual congress with loose women, I have never seen or had my attention called to a case of general paralysis among the vast numbers in the London County Asylums that showed a primary sore or a secondary rash. Krafft-Ebing noted the same fact, and concluded that the reason was that every paralytic had had syphilis and was therefore immune. He caused this hypothesis to be put to a crucial test. Nine cases of general paralysis were selected that gave no history and showed no signs on the body; these patients were inoculated with the virus of a typical hard chancre and watched for 180 days. They presented no signs of infection. The only assumption is that they were immune owing to previous infection, and that they possessed a power of resisting the action of the syphilitic virus. The concordance of this result with the statistical data of antecedent, inherited, or acquired syphilis in cases of tabes and general paralysis given later, led to the widespread acceptance by neurologists of the view that tabes spinalis or cerebri (general paralysis) is essentially of syphilitic origin. No syphilis, no tabes. Only a few eminent neurologists, such as von Leyden, refuse to accept the syphilitic origin of tabes, and one of the arguments employed against this view is that antisymphilitic remedies are of no avail in preventing the disease or arresting its progress. Moreover, we know that many people develop general paralysis or tabes dorsalis, even though they have been treated with mercury systematically from the primary infection onwards. So much has this impressed some authorities that they have even asserted that overmercurialization is the cause of the disease in question. The average time which elapses between the primary sore and the onset of tabes and general paralysis is, according to the observations of Schuster, the same in persons who have been thoroughly treated with mercury and those who have either not been treated at all, or only insufficiently. All the facts, therefore, go to prove that the syphilitic virus has in some way or other damaged the durability of the neurones, so that systems or communities die prematurely. It has been observed that Fournier includes other functional and organic diseases of the nervous system among the parasymphilitic affections. We have less knowledge concerning them and their pathogenesis. I have, however, seen cases of general paralysis in which the motor symptoms were most pronounced and the dementia slight, in which all the deep reflexes were exaggerated, and the plantar extensor reflex present on both sides—a very unusual occurrence in the ordinary paralytic dementia. At the autopsies there was a well-marked sclerosis of the crossed pyramidal tracts without any coarse lesion in the brain and cord to account for it. I have also seen cases of progressive amyotrophic lateral sclerosis occurring in the subjects of syphilis which appeared to be the result of the progressive degeneration of the whole motor efferent tract from cortex to periphery without any sensory disturbance. Some of the cases of Raymond cited by Fournier (*les affections parasymphilitiques*) with sensory troubles, namely, rheumatic pains and paraesthesiae, are obviously, from the account given of the appearances of the spinal cord *post mortem*, cases of subacute gummatous meningitis involving the roots. The serum diagnosis and the examination of the cerebro-spinal fluid bio-chemically and microscopically will permit us in future to determine whether syphilis is the essential cause of these degenerations. For every nervous disease, whether functional or organic, occurring in a person who has suffered from syphilis is not necessarily syphilitic in origin, yet when we consider the profound influence the virus has upon the blood and tissues of the whole body, it is not illogical to assume that any disease, local or constitutional, functional or organic, occurring

in a person who has acquired or inherited syphilis may possibly have found a suitable soil for development, owing to the diminished vital resistance of the tissues occasioned by such a potent and persistent poison as syphilis. Thus syphilis, although not a direct agent in such a case, by its devitalizing influence and the impoverishment of the lipoids, becomes an important indirect causal factor of the disease in question. There are many known ways in which syphilis can cause functional disturbances of the nervous system and lead to the development of neuroses and psychoses. The theory of the possibility of the syphilitic virus, or the lipid products of its activity, stimulating the neurones to increased dissimilative action and exhaustion, has been shown to have considerable support from recent investigations. There are, however, other conditions which are well known—namely, the change in the blood and blood vessels, and in the lymph and lymph channels. Long ago Virchow pointed out that in syphilis there is a diminution of red blood corpuscles and a hyperalbuminosis. Later, Schulgowski, Hafter, and Laacke described a considerable fall in the red blood corpuscle count. In the secondary stage Martin and Hiller, also Letzius, showed that not only is there a diminution in the number of red blood corpuscles, but also an absolute diminution of the haemoglobin content of the corpuscle. Anz found, besides the fall in number of the red blood corpuscles, an increase of the white, so that one can speak of a relative and absolute leucocytosis. Later observers showed that there was a diminution of polynuclear leucocytes, and that the leucocytosis was due to a great increase of lymphocytes, which increase we may associate with the polyadenitis. Further, there is an increase of eosinophiles. These changes in the blood in the secondary period increase in intensity with each fresh series of syphilitic manifestations, and diminish as they diminish; moreover, the blood changes disappear with the disappearance of the secondary symptoms under antisymphilitic treatment. Fournier long ago described the favourable influence of mercury upon the blood formation; clearly, then, the mercury, by its influence upon the productiveness of the syphilitic virus, allows a return of the normal haemopoietic formation, or arrests a too rapid haemolytic action. The French authorities were the first to call attention to a syphilitic anaemia, and to point out that iron had no influence thereon. The ebb and flow of the amount of oxyhaemoglobin is correlative to the flow and ebb of lymphocytes, which might indicate that, with the pouring out of an abundance of lymphocytes from the lymph stream into the blood stream, there was associated a pouring out of the virus that occasioned the irritation and hyperplasia of the lymph-cell elements. Hoffmann asserts that he has observed the serum of a syphilitic patient produce immobility and agglutination of the spirochaetes. Perchance it is that when the virus can no longer be neutralized by the defensive reaction of the blood serum embolic capillary effects are produced, causing papular eruptions of the skin, mucous tubercles, and occasionally meningitis. Selenow demonstrated blood changes before the outbreak of the secondary exanthem, therefore before the secondary incubation stage. It is probable that before the eruption becomes visible, microscopic changes have occurred in the affected cutaneous capillaries and adjacent skin structures, much in the same way as in the primary sore; consequently, we should expect a blood change to precede the eruption. The anaemia may be due to a haemolysis owing to an unloosening of lipid substances (lecithins and cholesterin) from the red corpuscles by the action of a toxic substance of the virus acting as a lyptic ferment disintegrating the osmotic membranes or by chemical interaction in the lecithin and cholesterin complex, forming the osmotic membrane producing physical changes by which the membrane becomes permeable even to the large haemoglobin molecules (Fig. 12). It may be supposed that the protein stroma of the corpuscle is covered by a film or membrane formed of this lipid substance, and the virus acts upon it in such a way as to dissolve, dissociate, or destroy the membranous film covering the corpuscle, and causing thereby a liberation of both the haemoglobin and the lipid substance into the serum. According to Levaditi and Yamanouchi, the lipoids serving for serum diagnosis not only exist in the liver, but in other organs, the brain and the red corpuscles.

They are probably complexes in which lecithin enters largely. The anaemia may, however, be due to interference with the functions of the haemopoietic tissues; in support of this is the fact, established experimentally by Neisser, that the red marrow and spleen are especially rich in the virus. Since mercury can rapidly improve this blood dyscrasia, it is probable that it does so by arresting the development of the *contagium vivum* in these blood-forming tissues. In congenital syphilitic children haemoglobinuria may occur, and this may be due to the existence of a large quantity of the virus in the blood causing haemolysis of the corpuscles. Many authorities working at the subject of metabolism in syphilis have shown that the nitrogen metabolism is altered. "Von Boick, Stephanow, and Bjelakow found that the assimilation of nitrogen of food sinks, and the percentage of extractives increases considerably in relation to the urea" (Max Nonne). This would indicate an altered dissimilative metabolism. There is therefore considerable evidence to show that causes exist which render the organs of the body more vulnerable, not only to other infective agencies—for example, tubercle causing scrofula—but also to the evolution and development of neuroses and degenerations by a devitalizing influence on the tissues by the unloosening of lipid substances. We have now to consider how far do these researches, biological and bio-chemical, help us in determining the etiology of tabes and general paralysis.

ETIOLOGY OF TABES.

(*Tabes Dorsalis, Tabes Optica, Tabo-Paralysis, General Paralysis.*)

The Wassermann method of diagnosis has come to strengthen and confirm the belief of many neurologists like myself: "*No syphilis, no tabes.*" This was previously based solely upon statistics and observations relating to the etiology of the disease. Moreover, the etiology and the serum diagnosis are reciprocally supporting not only of the parasyphilitic theory, but also of the view that there is one morbid entity which may be described as tabes—a view first put forward by Fournier, and which I have supported by comparing the clinical notes, and in a large number of instances the *post-mortem* results (with microscopic investigation) of 60 cases of tabes dorsalis and 60 cases of tabo-paralysis. I came to the conclusion that Fournier was justified in asserting the identical relation of the etiology, the close relationship and overlapping in the symptomatology and pathology, and that he was right when he destined them one day or other to be grouped in a single pathological entity; for Ferrier, in his admirable Lumleian Lectures on tabes dorsalis, says: "... and here I would express in concurrence with Fournier, Mott, and many other neuropathologists of the present day, my belief in the essential pathological identity of tabes and general paralysis. They are, in my opinion, merely different aspects of the same polymorphic disease." Both are tabetic, or wasting, affections of the sensory protoneurons in the one case, and of the cortical neurons in the other. The essential etiological factor is the same, and the average time elapsing between the primary infection and the onset of the degenerative process corresponds in the two diseases. Fournier remarks that the establishment of the syphilitic origin of tabes dorsalis, from his experience, would necessarily end in the application of the doctrine to general paralysis. In fact, there are so many symptoms in common and so many analogies of evolution and termination associating these two diseases, that it was quite natural to conclude the etiology of one from that of the other.

I have endeavoured to show in the *Archives of Neurology*, vols. i and ii, and elsewhere, all the evidence of the etiology of tabes and general paralysis tends to prove that there is in all probability one essential cause—syphilis, acquired or congenital; and that there are a number of contributing factors, any one of which by itself, or even in combination with others—for example, sexual excess, mental stress, heredity, injury, etc.—is not capable of producing the disease. The fact that congenital syphilis leads both to tabes and general paralysis at so early a period of life as to exclude most of the contributory factors except heredity, is an argument in favour of syphilis being the essential cause. Moreover, males and females are affected with juvenile optic tabes, tabes, and general paralysis in equal

numbers. Thus, of 500 general paralytics that have died and been examined *post mortem* at Claybury, there were 5 males and 5 females who suffered with juvenile general paralysis; that is, 2 per cent. of the total. The study of heredo-syphilis in relation to these parasyphilitic affections is especially convincing as to the essential cause of tabes and general paralysis being syphilis. This has been brought home to me in a very convincing manner in the large number of cases in which I have studied the family histories. I will cite a few examples: A young man was admitted to Claybury suffering with what were termed epileptic fits; the seizures did not cease, and he died; externally there was nothing on his body to show that he had congenital syphilis; his liver, however, showed typical signs of congenital syphilis, and the brain was typical of general paralysis. A brother in Caterham Asylum presented the facies of a typical congenital syphilitic. I ascertained that the father died of general paralysis, and the mother, when I interviewed her, was in the early stage of dementia. I was asked to see recently at Hanwell a young girl who, blind from optic atrophy, had later become demented. I was informed there were no signs of syphilis on the body, and she was one of a large grown-up family. Fortunately the mother was there at the time. I therefore had the opportunity of interrogating her. I found it was quite correct that she was one of a large family, but I also ascertained that, prior to the birth of this child, there had been several miscarriages and stillborn children, that this child had suffered with snuffles and a rash, that she had taken it to the hospital, and grey powders had been given. When the rash disappeared she ceased to attend further. As so often happens in these cases, the mother had not apparently suffered, and showed no signs of syphilis.

Another example I may mention. A juvenile paralytic boy was admitted to Bexley and died there. Recently his brother has been admitted with commencing signs of the disease. The former had Hutchinson teeth, but no history of syphilis could be obtained from the father. This man died in Guy's Hospital. I wrote to the registrar, and I received the information that he had had syphilis. Perhaps the most convincing case is the following one, which died in Claybury about a year ago. A boy was admitted with dementia, contraction of all four limbs, and epileptic seizures. Dying not long after admission, the *post-mortem* examination revealed very advanced general paralysis. There were no signs on the body, and the boy up to 12 years of age was bright and intelligent, then mental symptoms set in and steadily progressed. A history from the father showed that five years before marriage he had contracted syphilis, and, in spite of long treatment by an eminent physician, had not been cured, for the first child died within forty-eight hours of birth, the second within twenty-four hours, the third suffered with late interstitial keratitis, and later nerve deafness; then came the patient, and afterwards healthy children. I could multiply these instances, for altogether I have notes of some 60 cases, and in the great majority (over 80 per cent.) there are indubitable signs or an unquestionable history, as in the above cases, pointing to hereditary syphilis. I have found no case in which I could *certainly* exclude syphilis. Particularly common is optic atrophy, which takes these children to the blind school, and there they develop fits or signs of mental deterioration, and are next sent to the asylum.

The cases of tabes occurring in heredo-syphilis are not nearly so numerous as the cases of general paralysis; the ataxy is usually not very marked, optic atrophy is very common, and tabo-paralysis is met with often associated with optic atrophy; optic atrophy occurs also pretty frequently in the paralytic dementia of congenital syphilis. I have seen two brothers so affected, and die after developing the signs of progressive dementia.

The period of time elapsing between the evolution of tabes and general paralysis and the acquired infection varies considerably; it may be from three to thirty-one years; but the average is eight to fifteen years. The life of the neurons has been reduced, and the time that will elapse between infection and the onset of decay depends upon the intensity of the virus and the inborn resistance of the nervous system, together with other supplemental factors causing stress. In these hereditary cases it is surprising how frequently we find one of the parents, and occasionally both, suffering

from paralysis or tabes; this implies an inborn tendency to this degenerative condition. Now it may be asked, if twenty-five years, or even more, can elapse in an adult between the acquirement of syphilis and the onset of the symptoms of parasyphilis, why should not the same long period occur occasionally in congenital syphilitic cases, so that instead of the first symptoms commencing at puberty they are not manifest till adolescence, or even considerably later? Nonne relates a case of a workman, aged 32, who had suffered for two years with lightning pains and had never been infected with syphilis or addicted to drink, and who presented all the typical signs of ataxy. He had been treated in the hospital for severe hereditary syphilis. I have seen a somewhat similar case; moreover, I have occasionally observed similar cases of general paralysis—for example, a man aged 28 died recently in one of the London County Asylums of very advanced general paralysis. The disease was first manifested at the age of 18, when he had a fit. His character was strange; he married, had one child born dead, and afterwards his wife left him. He had no signs of syphilis on his body, but I found that his father had died eight years previously in Claybury Asylum. In my Croonian Lectures upon the Degeneration of the Neuron, I remarked that it is very probable that some of the cases occurring in adults in which syphilis can with certainty be excluded, may still owe the disease to an inherited syphilitic taint. It is not even necessary, as quite one-half of the juvenile cases show, that they should exhibit any external signs of congenital syphilis, for many of the juvenile cases which I collected were proved beyond doubt to be born of syphilitic parents, although manifesting themselves no external signs of syphilis, whereas brothers and sisters exhibited very definite signs. A case of general paralysis died at Banstead Asylum which had previously been under the care of Dr. Percy Smith at Bethlehem Hospital. This woman had characteristic signs of congenital syphilis, but she did not manifest symptoms of progressive dementia till she was 30 years of age. The patient was an unmarried woman, and there was no reason to believe that she had acquired the disease. Recently Christian Müller has put forward the same hypothesis to explain those cases in which no history of acquired syphilis can be obtained. He describes two cases of women (virgins) who were the subjects of well-marked signs of congenital syphilis, and who died of general paralysis at the ages of 42 and 43 years. The symptoms were not noticeable until a year or two before death.

Dr. Ferrier has in a masterly manner reviewed the evidence which points to syphilis being the essential cause of general paralysis and tabes, and, in conclusion, I cannot do better than quote him: "One might multiply arguments in favour of the causal relation between syphilis and tabes, but they are unnecessary. For those above related, singly and collectively, leave, in my opinion, little room for doubt that tabes and general paralysis are in all cases of syphilitic origin, and that tabes, *per se*, is as much a proof of antecedent syphilis as a gumma of the skin."

Although syphilis is the essential cause, yet, as Fournier showed, tabes and general paralysis are not syphilitic, but an outcome of syphilis, and the riddle is still unsolved why only about 3 to 5 per cent. of the persons infected with syphilis should subsequently suffer with one of these degenerations of the nervous system termed parasyphilitic. But only 10 to 15 per cent. of persons suffering with diphtheria develop post-diphtheritic paralysis; these are usually cases in which the local infective process was mild and often unnoticed; in that respect, like parasyphilitic affections, which more often than not follow mild and even unrecognized primary infection and secondary symptoms. Is it because the virus is attenuated or modified, and thereby has acquired a special neurotoxic action, or is it because in a small percentage of individuals the cells of the body, especially the cells of the nervous system, react to the virus in a hypersensitive manner? As already indicated, there are facts which suggest the possibility of a certain form of virus with a neurotoxic action. Thus Babinski remarks that it seems possible that a syphilitic virus may sometimes be endowed with a particular aptitude for attacking the nervous system; he reports the case of two students who were infected the same day by the same woman; both died fifteen years later of general paralysis; these students were, however, related. I have recently heard of two pro-

fessional men, not related, who acquired syphilis about the same time from the same nurse; ten years later they developed general paralysis. Marie and Bernhard relate the instance of two men who were infected from the same source, and ten years later suffered with tabes. Erb narrates an instance of four patients infected by the same woman, who later became the subjects of either tabes or general paralysis, whilst a fifth, who had connexion with the woman but was not infected, did not suffer with any disease later. Probably the most striking example supporting this theory of a special neurotoxic virus has been afforded by Brosius, who relates that seven glass-blowers suffered with chorea of the lip, and out of five who ten years later came under observation, four suffered with either tabes or general paralysis. If we accept the fact that a spirochaete is the specific causal agent of syphilis, it is conceivable that there may be varieties of this organism, as there are of the malarial parasite or trypanosome. Again, the organism may become attenuated or modified in its passage through the bodies of certain individuals, or it may be attenuated or modified by the action of mercury. It may thus happen that the virus may vary in different cases of infection. This, however, is speculation, and is not supported but rather contraindicated, so far, by experiments on animals. For although lower apes have the disease in a mild form when inoculated from the human being, yet the syphilitic virus of an infected *Macacus rhesus*, when used to infect a chimpanzee, appears to have lost none of its original virulence; for the chimpanzee suffers as badly as if it had been infected direct from the human source of the virus. We are probably, therefore, on more certain ground in attributing the variation of the effects which will follow infection not to the variation of the virus, but to the reaction of the individual himself, and we may represent this in the form of an equation:

$$\text{Symptom complex } x = \frac{V}{R} = \frac{\text{virus}}{\text{resistance}}.$$

If the virus V is constant, R resistance must vary. But R is made up of a number of factors, some of which we can ascertain, but it is generally impossible to decompose R into all its constituents. Roughly speaking, we may say that it is made up of what a man is born with, what has happened after birth, and what will happen in the future to resist the reaction of the specific virus, which in the majority of instances is of lifelong duration. Most authorities agree that with the widespread syphilization of a race for many generations, the disease tends to assume a milder form; the effects of the disease are not so severe, and a widespread tendency to an inherited immunity has been brought about. The conversion of a rural into an urban population has done much towards racial syphilization and to the diffusion of a tendency to inherited immunity, and the begetting thus of a mild form of disease. But, whereas there are fewer cases of severe syphilis than formerly, there are more cases of tabes and general paralysis. The interesting description given by Colonel Lamb of the syphilization of the natives of Uganda shows how severely a race previously free from this disease suffers from malignant skin, bone, and visceral disease. He also points out that tabes is very rarely seen. If we consider some facts concerning congenital syphilis, we must come to the conclusion that immunity is possible; how, otherwise, can we explain the law of Profeta, namely, the non-syphilitic child of a syphilitic mother does not acquire syphilis from the syphilized mother who suckles it? Again, the child may be syphilitic and the mother may show no signs of syphilis; the mother does not acquire syphilis by suckling that syphilitic child, whereas a wet nurse does. In the former case the fetus has acquired some antitoxin, or something from the maternal blood which has stimulated its own tissues to react against the virus; in the latter (Colles's law) the mother has derived from the blood of the syphilized child an antitoxin or something (not the living contagium) which has stimulated her tissues to react against the virus so effectively that she cannot be infected. There is no reason to suppose that the germ cells do not participate in this reaction, seeing that every cell in the body is subjected to the sensitizing influence of the chemical products of the virus by means of the blood and lymph. The experiments of Ehrlich have been quoted by Neisser as opposing the view of inherited immunity; on the

other hand, Conradi's recent experiments on lyssa support it. The histories I obtained in a large number of cases of juvenile general paralysis and cases of congenital syphilitic nervous disease revealed the fact that the mother very frequently had miscarriages, abortions, and typically syphilitic children without herself suffering at all, or presenting any signs of syphilis. In two instances the mother died of general paralysis; in a considerable number of instances the father died of this disease. As a general rule, the result of successive conceptions is as follows: Miscarriages, abortions, dead children, children dying in infancy—often of meningitis or hydrocephalus—children who later in life suffer with nervous affections—for example, nerve deafness, paralytic dementia, optic atrophy, and tabes—and, finally, healthy children. Such a chain of circumstances would undoubtedly indicate that either the virus was becoming attenuated or the resistance of its action was increased. In any case, we have reason to suppose that the children who were born with a syphilitic rash would be immune to reinfection, also those who afterwards suffered with parasyphilis; Krafft-Ebing's observation supports this premiss. It is probably a question of the degree of immunity to reinfection that would obtain in the presumably healthy children that followed the diseased ones. But such a chain of events does not always occur, for sometimes children are born with signs of heredo-syphilis after the birth of several healthy children; also parasyphilitic children may be born after the birth of several healthy children. This may be explained by the fact that the specific virus has become active again in the mother, which inference is negatived in most instances by the fact that she herself may say that she has been in good health, and no signs of the disease can be discovered in her. Another explanation offers itself, and it is that the specific virus may have attacked one ovum and spared another. Levaditi has seen the spirochaete within an ovum. No two individuals, even of the same family, are born alike, because the germ-plasm out of which they were formed may be similar, but is not the same; one inherits ancestral tendencies which the other does not; and it may happen, therefore, that a child born later than the healthy children possesses less inborn resistance to the action of the virus; consequently, manifests congenital syphilis or, later, parasyphilis. How can we explain this process of decay of particular groups, systems, and communities of neurons? Why should we have optic atrophy in one individual, atrophy of the spinal portion of the sensory protoneurons in another, decay and atrophy of the cortical neurons in a third, and, in many instances, a decay and atrophy of the whole nervous system? We cannot suppose that it is caused by the random metastasis of the syphilitic organism in the membranes, or coats of the blood vessels, conveyed by the lymph or blood stream, as is probably the case in the true syphilitic lesions of the brain and spinal cord. Everything points against this, for, although parasyphilitic affections present the most varied signs and symptoms, there is one sign usually present which is, for all practical purposes, only met with in parasyphilis, namely, the Argyll Robertson pupil. No coarse random lesion will explain the constancy of this phenomenon; moreover, this condition, although a sign of syphilitic infection, does not occur in true syphilitic brain disease. Spirochaetes have never been found in the cerebro-spinal fluid nor have antigens. Antibodies are found proportional to the extent of neuron decay in tabes and general paralysis.

I think all the facts are against the views of Lesser, Bose, and others, that these late manifestations of degeneration of the nervous system may be regarded as quaternary syphilis, a very late effect of the virus comparable with syphilitic orchitis, glossitis, and other sclerous lesions. According to this view, we should be compelled to consider the meningeal and perivascular infiltrations and the glia cell proliferation as the cause of the degeneration. But there are many reasons why we cannot accept this hypothesis. The view I take of the process is that parasyphilitic disease of the nervous system depends upon two factors, intrinsic, innate, and extrinsic, acquired—the soil and the seed; the vital resistance and the specificity of the virus, $\frac{V}{R}$.

All those conditions which may be inherited or acquired,

which tend to active metabolism of systems, communities, and groups of neurons functionally correlated, owing to those conditions of stress causing in one individual spinal neurasthenia, in another cerebral neurasthenia, will, in conjunction with the effect of the syphilitic poison, cause the nerve cells to exercise an abnormal dissimilative metabolic activity.

Ehrlich points out that we cannot suppose that the cells of the body possess *per se* an executive defensive capacity to neutralize the noxious effects of all forms of organisms, and his work on haemolysins shows that the haemolysin for the corpuscles of a particular animal only occurs after incorporation of the molecules of those corpuscles. But we may suppose that there is an *inherent* aptitude for the cells of the body of certain individuals to adapt themselves readily to defence against the action of the syphilitic virus in a race that has been widely syphilized for generations; consequently, a larger number will have a mild form of the disease. Cases of tabes and general paralysis occasionally arise within three years of the primary sore; possibly this may be due to an inherent hypersensibility to react to the poison. Dr. Byrom Bramwell has recorded a remarkable case of tabes which came on ten months after infection; it would be interesting to investigate the family history and past personal history of these cases to ascertain whether or not it was a second infection.

The nerve cells are perpetual elements incapable of regeneration, highly differentiated, and complex in structure and function; their centre of nutrition is the nucleus, and when decay sets in, the regressive process attacks first the fine twigs and branches of the tree, the dendrites and dendrons, and the rootlets; in fact, the process is an inversion of its growth and development. But what should cause this premature decay and lack of durability, for the specific energy of the whole of the neurons in the healthy body is sufficient to last until the vital spark dies out? We know the more prolonged duration of infectivity of the syphilitic virus as compared with other contagious diseases, also that one attack of syphilis confers immunity during the rest of the individual's life; moreover, the experiments of Krafft-Ebing are important to remember in this respect. The nerve elements being perpetual and having acquired a habit of increased metabolic activity, will continue it during life, and will contribute to the excess of lipoids in the blood. When there is no longer metabolic equilibrium, and decay sets in, these lipid proteid complexes are thrown off in increasing numbers; this seems probable from the fact that in general paralysis and tabes the quantities in the cerebro-spinal fluid increase with the progress of the decay. The process of decay will manifest itself in the earliest stages by an increased irritability and functional activity of the nervous structures, often manifesting itself in a *hyperaesthesia sexualis*, emotional exaltation and, not infrequently, in striking intellectual activity, followed in each case by exhaustion and loss of function. In my second lecture I referred to the fact that the lipoids may be products of nuclear activity and the highly *phosphorized* nuclein may be really the source of vital action. We can, therefore, understand how detrimental a *hyperaesthesia sexualis* is to the vitality of the body by the fact that it occasions a loss to the body by the sperm of nuclein substances highly charged with phosphorus.

The uselessness of antisiphilitic remedies is thus accounted for; indeed, they are generally positively injurious in true tabes and general paralysis because they lower the vital energy of a system which has over-immunized itself against the syphilitic virus. The only hope of doing any good is by an early diagnosis of the disease and suppression of all those exciting causes which use up the nervous energy and tend to overturn the normal metabolic equilibrium of the nervous structures. Other factors come in, determining the location of the degeneration, and although microbial infections and microbial toxæmias are not directly responsible for these parasyphilitic affections, yet they may be an exciting agent in the onset of the disease to the aggravation of the symptoms and the acceleration of the progress of neural decay and the fatal termination. I have often observed when influenza, dysentery, or pneumonia were prevalent in the asylums a number of general paralytics died after a succession of epileptiform or apoplectiform

seizures, and I have found, *post mortem*, that they were suffering from one of these morbid infections. It is a common thing to find on the *post-mortem* table patches of bronchopneumonia, the appearances of which would accord with clinical notes in the case-book reporting the occurrence of seizures; and, if the brain be examined microscopically, it is easy to prove that these fits may correspond with acute degenerative changes, doubtless caused partially by congestive stasis and partially by a toxic condition of the blood exciting and accelerating the process of neural decay. Bacterial invasion, *secondary or terminal*, of the organs of the body of a *non-specific* nature, therefore, may accelerate the morbid process of decay or bring about a fatal termination.

In conclusion, I thank the Fellows for their kind attention, for I am not unmindful of the fact that many distinguished men have preceded me in the delivery of the Morison lectures. I feel that I have dealt imperfectly with a very difficult albeit important subject still in its infancy; and I can only hope that the words of the old philosopher, Lucretius, may come true, "that one thing after another will grow clear, and dark night will not rob you of the road, to keep you from surveying the utmost things of Nature; in such wise things will light the torch for other things."

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A CASE OF ACUTE ASCENDING PARALYSIS.

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LANDRY'S disease is sufficiently uncommon to make the report of a case which recently came under my care worthy of publication.

The patient, a man aged 24 years, had had no illness during the last few years, except an occasional cold, which did not incapacitate him from work. He got wet cycling a week previous to my seeing him, but followed his occupation during the next four days and did not feel at all unwell; on the fifth day he remained at home complaining of vague pains and a feeling of general weakness. He did not improve, and I saw him two days later.

I found him sitting on a couch downstairs still complaining of pains in his shoulders, legs, and back, the latter being the most severe and referred to the sacral region. He also complained of a feeling of numbness from the middle of the body down to the feet and of weakness in the legs, but there was no girdle pain, nor at this time any definite paralysis. He could rise up from the couch and stand or walk without assistance, but said he did not feel safe on his feet. There was no difficulty in breathing or swallowing, and no rise of temperature. The knee-jerks were entirely absent.

The next day he still had pain in the back and said it felt weak, and the weakness in the legs had progressed to a definite paralysis, so that he could not get up or stand without assistance. Both legs and feet were affected to about the same extent, but, judging from the slight motion remaining, the posterior muscles were paralysed to a greater extent than the anterior. He was unable to turn over in bed and felt easier in a chair, where he sat huddled up, often requiring support to maintain his position or help in changing it. He now complained of some weakness in the arms, and his voice was weak

and husky; he had some difficulty in clearing the throat, and cough was wanting in energy, and there was some difficulty in swallowing. The abdominal muscles were flaccid, and seemed to have lost power, and probably the intercostals, the quadratus lumborum, and the muscles of forced expiration were beginning to share in the paralysis. The movements of the chest were impaired, but there was no dyspnoea. Sensation in the paralysed parts was unaffected: he could feel the slightest touch of a pin or the finger, and pain when pricked with a pin. The muscles felt of normal firmness, and were not tender when handled.

On the third day the paralysis had rapidly extended; the legs were almost motionless, but he was still able slightly to extend them at the knees. He begged to be out of bed, and sat more huddled up from paralysis of the back and abdominal muscles, and had to be supported by pillows, or, when I saw him, by a friend on either side. He was unable to raise the arms at the shoulders, but could flex and extend the elbows, although not able to hold a cup with his fingers or to carry it to his mouth. His head hung forward. He spoke in a whisper, but beyond that the speech was not affected, and no paralysis of the tongue, lips, or face was observed. The loss of voice was probably due in a great measure to paralysis of the expiratory muscles. He had great difficulty in clearing the throat of secretion, the power to cough and all expiratory efforts being almost entirely lost. There was much trouble in swallowing, but no regurgitation of fluid through the nose, and the soft palate, as far as could be judged, was not affected, the dysphagia being due to paralysis of the muscles presiding over the act of swallowing. He was able to swallow small pieces of jelly better than liquids. He had no marked dyspnoea and no violent respiratory struggles. No ocular paralysis was observed. About 11 p.m. he was almost asphyxiated by the accumulated secretion in the throat which he was unable to expel.

On the fourth day I found he had passed a very bad night, the secretions in the throat causing much distress. He could not clear his throat, and swabs or sponges had to be used. He lay almost motionless, and during the day became rapidly worse. The movements of the chest were quicker and feebler, and the paralysis affected the respiratory muscles—pharynx and larynx—more and more. Swallowing became exceedingly difficult, but he was still able to take a little jelly. His mental faculties were quite clear, and down to this time the temperature was never half a degree above normal. At 10 p.m. it rose to 102°.

He died quite suddenly about 1 a.m. next morning. About half an hour before death the sphincter became paralysed and he passed faeces involuntarily. There was no convulsion or struggling, and his mental condition was quite clear to the end; in fact, he made himself understood to the nurse within a few minutes of death, which appears to have been due to asphyxia.

No treatment seemed of any avail. An autopsy was not obtainable.

The chief features of the case, apart from its rapid progress, were:

1. No obvious cause, beyond getting wet.
2. Absence of knee-jerks from the onset, before any actual paralysis was noticed.
3. No rise of temperature until within three hours of death.
4. Sensation unimpaired, the only sensory symptoms being numbness and vague muscular pains.
5. Perfect consciousness of his state to the end.
6. Rapidity with which the paralysis affected the acts of coughing, all expiratory efforts, and swallowing.

With regard to the order of invasion, after the feet and legs became paralysed the progress of the disease was so rapid that it was difficult to follow the exact sequence, except (a) the posterior muscles of the legs and thighs appeared to be affected before the anterior or to a greater extent, and (b) the muscles moving the upper arm on the scapula before those of the forearm.

As a note of distinction from acute disseminated myelitis I would mention (1) the absence of anaesthesia or any impairment of sensation; (2) normal temperature except just before death; (3) the freedom of the rectum and bladder until within half an hour of the end.

THE reports on the therapeutic results with radium which have come from Germany seem scarcely so optimistic as those from Paris. Dr. H. E. Schmidt of Berlin (*Jahrbuch ueber physikalischen Medizin*, p. 193) says that in all cases of naevus treated by him he has always found a tendency in course of time for the redevelopment of telangiectases, generally some months after the discontinuance of the treatment, and he believes that in such cases treatment by Finsen light or electrolysis is necessary to complete the cure. He speaks of one specially good result which he obtained in a case of naevus pigmentosus pilosus in a child. The growth was on the left cheek, about the size of a shilling, dark brown, and hairy. After prolonged treatment the naevus disappeared, leaving only a not very noticeable scar, but here and there dilated vessels began to appear in it, yet by following up the cure with Finsen-light treatment most of these dilated vessels were removed, and the final result was very good.