example of truly somatogenic acquirement of an inherited and inheritable constitutional state.

Defect in bodily metabolism has led to intoxication of the germ cells, and the offspring show a peculiar liability to be the subjects of intoxications of the same order. Here what is transmitted is a constitutional state, and that constitutional state may manifest itself in more than one way, but no one will deny that this is truly inheritance of an acquired condition. We must therefore, I hold, be prepared to admit the transmission of inheritance of certain orders of acquired constitutional conditions. We must see that it is not necessary with Weismann to deny strenuously the inheritance of each and every order of acquired defect, and that along the lines of some such theory as that outlined this evening, we gain a fuller harmony between theoretical considerations regarding the nature of inheritance and the facts as they present themselves to us day after day.

REFERENCES.

¹ Weismann, *On Heredity*, authorised translation by Poulton, Schönland, and Shipley, Oxford, 1889, p. 413. ² *Loc. cit.*, p. 170. ³ Weismann, *On Heredity*, p. 410.

THE PATHOGENESIS OF TABES AND ALLIED CONDITIONS IN THE CORD.

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If the etiology of tabes were accurately determined, a large and important chapter in neurology could be written. Two sets of views prevail. The view generally held regards the degeneration of the neuron as primary, and the affections of the connective tissue, vessels, and neuroglia as secondary, in importance. A few writers hold another view, directly negative of the first. According to them, the primary affection is to be found in the vascular connective tissue in which the nerve fibres lie. This constitutes what is known as the vascular theory of the disease, and the various considerations in its favour and against it have from time to time been keenly discussed. In 1880 Adamkiewicz proposed to explain all cases of tabes in this way; a few years later he concluded definitely that some cases were parenchymatous in origin. Records of isolated cases have been published, notably of cases in their early stages, in which the vascular origin of the disease has been clearly established. But while the accuracy of these observations has not been questioned, the cases recorded have been regarded as accidental, and they have not shaken the commonly-received opinion. Some living authorities entertain the vascular theory in a modified form—namely, with regard to the nutrition of the posterior nerve roots (Redlich and Obersteiner). But, on the whole, it receives little support, as may be seen by a perusal of recent discussions and important writings on the subject.

At a discussion on tabes by the London Pathological Society in 1899, reference to the vascular theory was confined to one or two speakers, who hinted that perhaps too much was taken for granted with regard to the secondary importance of the vessels. The same thing occurred two years ago at a discussion in the New York Neurological Society, and no greater deference is shown to the theory in a recent critical summary of views upon the subject of tabes by Soury,¹ who, however, gives clear expression to an opinion which is pretty universally held, when he states that the old view which regarded tabes as a disease of the posterior columns, or even as a disease of the cord itself, must be abandoned. It is to be regarded, he says, as a disease of the central nervous system. This marks a distinct advance upon earlier conceptions. Put shortly, then, tabes is now almost universally regarded as a primary disease of the nervous system. The general position is thus defined by Gowers:

The great fact of the pathology of tabes is that it is a neural degeneration in the sensory nervous system, peripheral and central. . . . The degeneration commences in the nerve elements themselves, the overgrowth of connective tissue which gives to the lesion its characteristic features is secondary.

The views advanced in this paper bring me into line with those who support the vascular origin of the disease, as opposed to those who hold that the nervous elements are primarily affected. I do not propose to discuss the condition

of the cells in the posterior root ganglia, nor the condition of the membranes over the posterior columns and nerve roots, as the inconstancy of these changes is admittedly so great as to indicate that they cannot reasonably be considered to have primary significance. Moreover, the experimental work of Lugaro, corroborated by that of Marinesco, van Gehuchten, and others, has shown that section of the posterior nerve roots, and even of the columns themselves, does not morphologically affect the posterior root ganglion cells. It will probably conduce to clearness if I preface my detailed argument by a brief outline of the position I occupy. I hold that tabes is not a "nervous" disease in the sense usually apprehended, and that the lesions in and around the vessels are of primary importance, the lesions of the neurons being determined by local interference with the blood supply. (This does not exclude the consideration of a varying vitality of neurons as an important factor in the disease.) Further, there is, I think, good ground for the belief that the condition is dependent on a chronic autointoxication, the vascular lesions being to some extent general, but tending to be more advanced locally, and that the more advanced local changes determine a failure of nutrition in the adjacent nerve elements. If these views are correct, it appears to me that the condition ought to be curable in the early stages, and further, that the present tendency to differentiate tabes sharply from many other diseases in which there is a well-marked lesion of the cord of an allied character is to be deprecated. We should rather investigate the nature of different toxins and the conditions which have brought about variations in the results of their action.

COMPARATIVE PATHOLOGY.

The importance of the study of comparative pathology for the elucidation of problems in the etiology of nervous affections in the human subject is hardly sufficiently realised. It is more than probable that a close study of nervous disorders in lower animals would contribute largely to our knowledge of the causation of allied diseases in man. Until recently no attempt has been made to give a systematic account of any disease of the nervous system in domestic animals. While the existence of such diseases has been inferred from observation of symptoms during life, complete pathological records are wanting, and even the clinical descriptions of these supposed nervous disorders, given in standard veterinary works, are extremely vague and unsatisfactory.

Some time ago I had an opportunity of observing a horse affected with ataxia, paraplegia, and a bilateral affection of the knee-joints of a nature not described in veterinary literature. The combination of clinical features led me to diagnose a lesion of the cord, most marked in the posterior columns, with associated neurotrophic joint lesions, of a nature akin to tabes in the human subject. The lesions found at the *post-mortem* examination were of a grosser and more widespread nature than had been anticipated, but the diagnosis was found to be substantially correct.² Special emphasis is laid on the greater proclivity of the vessels in the posterior part of the cord to be affected with an extreme degree of hyaline and fibroid thickening, and it is suggested that the process is due to some toxic action. I am aware that, even if this suggestion were established as correct, its value as a contribution to the etiology of tabes depends upon the existence of a real relationship between tabes and the pathological condition described. I believe that such a relation exists, and that, if due regard is paid to the different life-histories and habits of the two subjects, the nervous disorder in the horse throws a direct and important light on its analogue in the human subject. This opinion may be corroborated by the striking fact that the clinical appearances arising from the disturbance of the muscular sense in the lower animal correspond in the main to those encountered in man. The features presented in the early stages of such a disturbance are well represented by Fig. A. The animal shows an unnatural position of the hind limbs, which are more spread out than is natural, and an undue prominence of the knee-joint with slight eversion of the limb is apparent. The fore legs also are unduly wide apart. The condition of the joint referred to is due to loss of muscle tone, and probably also to direct relaxation of the joint structures. Although this

animal does not, strictly speaking, represent the class of disease at present under consideration, it is perhaps none the less interesting. It is probably a unique case. Five weeks before this photograph was taken the animal was the subject of a severe cerebral thrombosis. It was perfectly unconscious for twenty-four hours, and within four days very extensive bilateral skin lesions of a so-called "trophic" nature developed at all the points subject to pressure. The extensive areas of ulceration visible on the side of the abdomen and over the shoulder represent little more than a half of the originally-affected areas. Similar lesions were present on the hind quarters. It is interesting to note that this animal is now exhibiting the early indications of "stringhalt," a disease familiar to veterinarians, and which I have elsewhere suggested is due in many cases to an affection of the lateral columns, similar to lateral sclerosis in the human subject.

In a later contribution³ I have described a case of nervous disorder in a young subject, a hackney, aged 18 months. Its symptoms—ataxia, paraplegia, etc.—led me to diagnose the condition as one allied to Friedrich's ataxia in the human subject. The post-mortem examination substantially confirmed the diagnosis. Plates 9 and 10 illustrate some of the features of this case. The former shows a very pronounced degree of vascular disease in the periphery of the lateral column, where the nerve fibres were extensively degenerated; it also shows a large number of small spaces, more or less circular in form—dilated perivascular lymphatic spaces. The latter shows an area of softening in the postero-external columns of the same section with marked fibroid thickening of vessels, both in the midst of the softened area and at some little distance from it.

The significance of these changes and their relation to nervous diseases in the human subject will be dealt with later, but it is important to observe that the pathological record of the case shows the nerve lesions to have been the direct result of vascular disease in the affected areas. I have expressed the opinion that this vascular disease was itself dependent on a chronic pre-existing toxæmia, probably closely associated with mal-assimilation in the digestive tract, a condition which ought to be curable in the early stages of disorder. It should be mentioned that in this case also the vessels in the posterior part of the cord were most affected.

In a recent number of the *Veterinary Record* (March 23rd, 1901) there is a very interesting clinical record of four cases of "locomotor ataxia," by J. J. Vahey, co. Mayo. The first two cases—a yearling colt and a two-year-old filly, a half-sister of the colt—exhibited marked symptoms of inco-ordination, paralysis, immobility of the pupil to light, etc., the disease running a progressive course and necessitating the destruction of the animals within eight months after the initial symptoms had been observed. There was no post-mortem examination.

The remaining two cases were even more interesting, the one being a yearling colt, the other a two-year-old filly, full sister of the colt. These exhibited symptoms similar to those observed in the early stages of the other cases, but after some months gradually recovered, or, as the author admirably expresses it, "they were restored to usefulness."

The great interest of this record led me to take an opportunity of seeing the author and I was able thoroughly to satisfy myself, so far as that is possible of anything that has not come under direct personal observation, of the accuracy of the record.

The age and relationship of these subjects, and the clinical features and course of the disease in the two sets of cases, are specially interesting in the light of the pathological record of the hackney already referred to. With regard to the recoveries I think it reasonable to conclude that one of two things occurred: (1) The toxins disappeared from the tissues, or diminished sufficiently to lead to the disappearance of symptoms; in other words, a diminished absorption took place; or (2) the resisting power of the animals increased, due to a gradually-acquired immunity.

Can any further evidence be adduced in favour of these views? I believe that some facts of experimental pathology furnish additional evidence, and will briefly refer to a series of observations at which I have been engaged for the past year. This investigation, carried out in the physiological department of the University, was primarily an experimental study in 'gout,' and, as the research is not complete, I merely wish to refer to the occurrence of certain nervous symptoms observed in its course. The subjects under investigation were common barn-yard fowls, fed on a diet strictly limited to red meat and water. At the end of nine months, at which period the experiments were partially concluded, the subjects for our present purpose were divisible into three groups:

A. Those (two in number) which had succumbed, or of necessity been

killed, within three months and a-half of the commencement of the special feeding. The symptoms observed were of an acute nature, ataxia, paraplegia, gradually developing unconsciousness, and death within four days of the onset of symptoms.

B. Those (five in number) which had exhibited no nervous symptoms of a similar profound nature.

C. One hen, which was at this time in fair health, but which had at different periods experienced two severe attacks of a nature precisely similar to those recorded in Group A, without, however, involvement of the higher neurons.

There was no trace of diminished consciousness nor other indications of cerebral disturbance, but in other respects the symptoms were similar. At the time of the attack no change was made in the dietetic or other régime, the only difference being that the animal ate very sparingly for several days. The fowl recovered slowly on each occasion in from eight to ten days, and was killed three months later on the occurrence of a third more severe attack. In this case also I believe that the previous recoveries were mainly due to the acquisition of some degree of immunity to the action of the toxic substance or substances responsible for the symptoms. I further believe that in man recoveries from nervous symptoms of a toxic origin, fairly comparable to the foregoing, are by no means infrequent, but on account of the accepted theory which has made the vascular disease a relatively unimportant symptom, the significance of these recoveries has been totally misapprehended.

EARLY TABES.

The second point to be determined is how far do the histological appearances of the cord in early tabes justify the view that the primary lesion is to be found outside the nerve elements. By early cases I mean those that have been submitted to histological investigation any time within a few years of the onset of symptoms sufficiently pronounced to lead the patient to come under medical observation. I add this last qualifying clause for a special reason. No one will, I think, deny that we cannot regard the first recognition of early symptoms—for example, loss of knee-jerks, as synchronous with the onset of the disease. We are then merely dealing with the first gross expression of a disease that had been latent for some time previously. We find certain difficulties on the very threshold of this inquiry. Post-mortem records of early tabes are very rare, and of these some at least appear to have been investigated from the limited standpoint of nerve degeneration, and are therefore valueless for the present purpose. Other records are of comparatively little value, as they give little indication of the exact degree of vascular disease. Terms like "advanced," "well-marked," and "slight," and their equivalents in other languages, hardly convey sufficient information, especially when applied, as they often are, to the blood vessels as a whole, without any reference to their minuter terminations. For this reason I lay special stress on the admirable histological reports of the following cases of early tabes, which clearly indicate the thoroughness of the investigation.

Buzzard has described in *Brain*, vol. vi, 1884, under the title Posterior Spinal Sclerosis consecutive to Disease of Blood Vessels, a case of tabes in a man aged 39, in whom symptoms had been present for 27 months before death. To quote from his description: "The symptoms during life confirmed by the appearances after death point conclusively to tabes dorsalis..... The lesions point to a peri-arteritis apparently originating in the soft membranes and spreading inwards along the nutrient supply of the posterior columns. That the disease had not remained strictly confined to these columns but had spread, though in far less degree, to other parts of the cord, is what may often be seen in cases of tabes." He later raises the important question whether we can allow the probability that the disease is sometimes the result of changes in the connective tissues bringing about destruction of nerve tubes, and at other times originates in the nerve tubes and spreads to the connective tissue.

This record gains in interest from a later one by Bullen (*Brain*, vol. xi, 1888), who records a case of locomotor ataxia followed by general paralysis of the insane. The patient was a man, aged 24, who died within 33 months of the onset of symptoms. Like the record by Bevan Lewis in Buzzard's case, the histological description of this case is extremely interesting. In addition to the main lesions in the posterior columns, there was sclerosis with marginal degeneration of the lateral columns and marked changes in the anterior and posterior cornua, the lesions being dependent on disease of the vessels. But this observer found that the conditions of the investing membranes did not lend any support to the theory of the origin in the membranes of inflammatory action, which might have spread along the arteries.

In a further communication the same author⁴ records a similar case in a man aged 33, in whom the disease ran a rapid course, and where the histological picture was similar to that in the previous case. The commissural zones and also the lateral columns were markedly involved.

Buzzard⁵ describes a case of tabes with ophthalmoplegia externa in a man aged 36, the subject of heart disease. Here the lesions were limited to the posterior columns and the posterior cornua, the latter

being described as the seat of grey degeneration and a small cavity. There was also a lesion of the pons in the neighbourhood of the sixth nucleus, which was "obviously vascular in origin." Here again, therefore, we find evidence in the small cavity formation and in the nuclear lesion of an important vascular affection, which favours the view that the other lesions in the same case were of similar origin.

I have lately had the opportunity of examining a small piece of the cord from a case of tabes of two years' duration in a patient who died from malignant disease. Here also the evidence was confirmatory of the primary importance of vascular disease. The degree of vascular change was profound, and the degeneration of the nerve structures, as indicated by the amount of softening, was more acute than obtains in cases of uncomplicated tabes, and I believe that in such a case we find additional proof of the general view advanced in this paper. Given an added toxæmia such as is present in malignant disease, the result will be an added severity in the local lesions throughout the cord, and these will be correspondingly greater in that part of the cord which, in our opinion, is more susceptible to various toxic influences. In the same way I believe that in cases which run an acute course, a careful investigation of the history will reveal the previous occurrence of conditions similarly capable of so influencing the tissues as to render them more susceptible to the influence of the toxins at work.

Other records might be cited such as those of Krauss favouring the vascular origin. I have not been able to find records of any case in which vascular disease was absent.

ADVANCED TABES.

This brings me now to the third point in the investigation. Can any evidence be adduced from the histological study of cases of advanced tabes in support of the view that the primary fault is to be found in malnutrition rather than in a primary degeneration of the nervous elements? I believe so. In the following record I have deemed it advisable to draw my illustrations from, and confine my remarks to, a single case, as we thereby secure a greater continuity of thought with regard to the process at work. I may, however, state that the evidence derived from an exhaustive examination of the cord in the case chosen, when compared with the descrip-

tions quoted in standard textbooks and writings, and taken along with the results of similar investigations, showed that I was dealing with a case that perfectly conformed to the recognised description of the disease. The patient had been an inmate of Hawkhead Asylum, having been admitted on account of mental symptoms supervening in the course of

well-marked tabes dorsalis. The classical features of this disease were present on his admission to the asylum. As the alterations in the medullated nerve tracts of the cord were also characteristic, it is unnecessary to describe them in detail. I shall merely draw attention to those appearances which have a bearing on the special points under consideration.

In Fig. 1 the advanced degeneration of the posterior columns and slight involvement of the lateral tracts are well brought out, the disease in the lateral columns being most marked at the periphery. As is not infrequent, however, in such a low magnification, the actual degree of involvement of the lateral columns is in-

adequately brought out, and for the same reason the distinct involvement of the anterior part of the cord, as shown in Fig. 3, is not brought out at all in the illustration. The

cornu-commissural fibres appear to have escaped, but when we turn to Fig. 2 we find that their escape is more apparent than real. This illustration clearly shows the existence of a diffuse degeneration throughout these tracts, many of the fibres being completely degenerated. It also shows a vessel (a vein) in the deeper part of the median septum in a state of marked dilatation with slightly thickened walls, a histological feature which I have noted in other cases of tabes, and have also seen referred to by other observers. Not only are very many of the cornu-commissural fibres degenerated, but an examination of the vertical section of the posterior columns both in its deeper and its superficial parts shows that many of the fibres which appear to be healthy are not really

so. It can be frequently observed that their axis cylinders show a marked degree of irregular swelling and tortuosity that clearly indicate a diseased state. Fig. 1 appeared to indicate that the anterior part of the cord is healthy, but it is not so. It is the seat of a decided

Fig. A.—An ataxic horse. The position of the hind limbs is abnormal. The limbs are too far apart, and the limb nearest the onlooker is everted; the knee-joint is unduly prominent, indicated by the light shading.

Fig. 1.—Weigert-Pal. $\times 8$. To show the typical appearances of the cord in advanced tabes. The lateral columns are seen to be involved. The cornu-commissural tract and the anterior columns are apparently healthy, but are not so. See text and Figs. 2 and 3.

Fig. 2.—A higher magnification of the cornu-commissural tract of Fig. 1; shows diffuse degeneration extending down to the grey matter. (Hæmatoxylin and eosin. $\times 60$).

Fig. 4.—Peripheral part of one lateral column from the lumbar region. Note the number of greatly-thickened vessels visible throughout the field. Cf. No. 9 taken from the horse. (Hæmatoxylin and eosin. $\times 60$).

Fig. 3.—A higher magnification of the anterior columns of Fig. 1; shows diffuse marginal degeneration of the nerve fibres. (Hæmatoxylin and eosin. $\times 60$).

Fig. 5.—Posterior columns. (Hæmatoxylin and eosin. $\times 200$). To show the nature of the vascular disease. The arteriole to the right shows marked hyaline fibroid thickening, with considerable diminution of the lumen.

Fig. 6.—Sacral cord—posterior columns—shows an area of atrophic softening with remains of diseased vessels in relation to it. Cf. No. 10, which shows a similar appearance in the horse. (Hæmatoxylin and eosin. $\times 100$).

Fig. 9.—Horse, aged 18 months. Peripheral part of lateral column (hæmatoxylin and eosin. $\times 55$). Note the pronounced thickening of many vessels throughout the field; also the dilated perivascular spaces, and compare the same in vertical section of the human cord in tabes, Fig. 7.

Fig. 8.—Anterior cornu, cervical region. (Methyl violet. $\times 300$). To show pronounced neuroglial overgrowth similar to what occurs in the brain in general paralysis.

Fig. 10.—Horse, aged 18 months. (Hæmatoxylin and eosin. $\times 100$.) To show an area of softening in the posterior columns in the same sections as Fig. 9. The remains of thickened vessels are seen in the cavity. Below are seen some vessels showing advanced fibroid thickening.

marginal degeneration of nerve fibres that is fairly well brought out in Fig. 3. The degeneration extends down the anterior columns along the central fissure. (The reader may have observed that Figs. 2 and 3 are noted as stained with hæmatoxylin and not with one of the ordinary nerve-fibre stains, the reason being that hæmatoxylin gave, somewhat unexpectedly, a beautiful nerve-fibre stain. Other methods gave corroborative results, but not quite so sharp differentiation). These figures demonstrate that the involvement of the cord is in reality a very extensive one, and in my opinion the changes in the various columns differ merely in degree. Now look for a moment at the state of the vessels in the affected areas. Fig. 4 shows the periphery of the lateral column on the side on which there is a greater degeneration of nerve fibres. Many greatly-thickened vessels are seen throughout the field, and an examination of the capillaries likewise shows extensive thickening, with diminution of the lumen, sometimes to obliteration.

Comparative pathology provides an illustration in Fig. 9 of the same phenomena. That picture is taken from the case of the young hackney already referred to as a case of Friedreich's ataxia. It represents the peripheral part of the lateral column on one side at a part of the cervical cord where there is marked degeneration of nerve fibres in these columns. Everywhere there is a marked overgrowth of the vessel walls. These observations of degeneration in the nerve fibres of the lateral columns, and of a great simultaneous change in the vascular condition over the whole field, are corroborated by the admirable histological records of early tabes supplied by Buzzard and Bullen. Their significance can scarcely be over-estimated when it is remembered that the prevailing theory of the causation of tabes owed its acceptance in part to the belief that degeneration of the nerve fibre was almost confined to the posterior columns, and in part to the fancied disproportion throughout the whole course of the disease between the vascular changes and the changes of nerve fibre, leading to the inference that the former were of secondary importance. As I have already said, it is now universally admitted that tabes is not to be described as a disease of the posterior columns, but the second pillar of the neuronie theory of the disease is still generally upheld.

The spaces which appear in Fig. 9 also deserve consideration. Hitherto when similar appearances have been encountered in cases of tabes in the human subject, they have been described as dilated perivascular lymphatics. It is probable that this is the correct explanation of most, but hardly of all. In some cases they are, I think, mere dilatations of lymphatic spaces, determined by traction of the cirrhotic tissue around, and in others they represent spaces from which nerve fibres have disappeared. In the main, however, they represent much dilated perivascular lymphatic spaces, as is readily proved by study of a vertical section (Fig. 7) of the posterior columns of the case of tabes under consideration. In that figure it will be noticed that one of the vessels is in the act of falling out, two spaces contain their respective vessels, and in others the vessels have previously disappeared. The capillaries are seen to be much thickened; with this method of staining, a healthy capillary should not stand out above the surrounding tissue. The large number of amyloid bodies seen throughout the field are significant of a long-continued toxic action on the cells in question. When the arterioles are examined with the high power (Fig. 5), the striking change is seen to be a hyaline fibroid thickening, which causes a marked narrowing of the lumen, sometimes to complete obliteration. This change affects all the coats of the vessel. In some cases it is impossible to accurately differentiate the particular part of the vessel primarily or mainly affected. Nor, it seems to me, is it in the least degree necessary that we should do so. Indeed, I think that a more helpful conception of these conditions will be obtained if we regard the smaller vessels as merely composed of one structure—namely, connective tissue permeated by muscle and elastic fibre, and lined by endothelium. Whether that be so or not, it is difficult to resist the conclusion that the nature and extent of the changes disclosed by the various figures indicate vascular disease as the primary disorder. More especially is this the case when it is remembered that disease of the vessels induced by the long-continued action of some irritant will cause defective nutrition of the related cord, and

that defective nutrition accounts simply and adequately for degeneration of the nerve fibres, while in my opinion the converse is not true. I believe that the past failure to see the true causal relation between the vascular changes and the nerve degeneration has been due to the unfortunate elevation of the latter to the place of first importance. The due correlation of the two not only removes the vascular disease from the category of inadequately explained concomitants, but, by tracing the degeneration of nerve fibres to the operation of that disease, suggests the possibility of a more rational and successful treatment of "nervous" disorders. If, on the other hand, the generally-accepted view of tabes were correct, the degeneration of the neuron being primary and the vascular change secondary, then in other conditions where there is a primary degeneration of the nerve fibre we should expect to find a proportionate degree of vascular disease. In one case which I have had the opportunity of examining—a case of hemiplegia of many years' duration—the degree of vascular disease in the lateral columns was not in excess of that found in the unaffected parts, and did not compare with the degree present in the cases of tabes examined. The only observations on this point, other than experimental, which I have been able to discover are those of Krauss,⁹ who found that of 4 cases 2 showed slight, and 2 showed considerable, changes in the vessels. His general conclusion was that there was no pronounced vessel change in his cases of secondary degeneration. (It is, however, right to add that he considered that in this respect there was no essential difference between them and tabes.)

Fig. 7.—Vertical section of posterior columns in lumbar region ($\times 46$). Note the dilated perivascular spaces, and compare Fig. 9 from the horse, where the same are seen on transverse section. The dark lines visible throughout the field are diseased capillaries. The small black dots are amyloid bodies. (Palladium methyl violet method.)

The character of the lesions produced in the larger and smaller vessels depends on many features, but especially on the nature and rapidity of the toxin at work. Fig. 6 shows an area of atrophic softening in the posterior part of the sacral cord, and in this connection it may be mentioned that the vascular disease in the sacral cord was specially advanced, and was pronounced in the anterior as well as in the posterior part of the cord. A few similar areas of softening were found elsewhere both in the grey and white matter. If we turn to comparative pathology we find in Fig. 10 identical lesions in the posterior columns. This illustration shows above an irregular area of atrophic softening, the remains of diseased vessels being obvious in the debris, and below are seen larger vessels in a state of advanced fibroid degeneration. As I indicated in an

earlier part of this paper, when comparing the *post-mortem* features of these diseases in animals with those in man, we must have due regard to certain factors, which might naturally be expected to modify the histological appearances in the two cases. When we consider the different circumstances under which the two subjects live and work, it is, I think, reasonable to believe that such a pathological process as we have been considering would tend, in the horse, to run a more rapid course than it does in the human being, and my observations tend to show that this is what does occur.

There is only one other point calling for consideration. Fig. 8 is most instructive. We find in the grey matter a varying degree of neuroglial overgrowth well brought out in the illustration. This is precisely the condition which occurs in the cells of the grey matter in the cortex in general paralysis, and is associated with, and, indeed, dependent on vascular changes in the small vessels supplying these areas. This relationship is admirably brought out by a study of vertical sections of the cord (methyl-violet method), where we can see that the different areas of sclerosis have a small vessel in their midst.

Having now shown that the facts of comparative pathology, so far as they have been ascertained, lend support to the vascular theory; and that the facts disclosed by the detailed histological investigation of some cases of early tabes point irresistibly to the same conclusion, while we have no record of cases where the vascular origin of the disease can be definitely excluded; and having in the last place shown that an exhaustive and unprejudiced examination of advanced cases yields confirmatory results, we now pass to the clinical standpoint, and ask whether the theory is supported by the experience of the physician. If the minute records of actual practice show facts which are utterly inconsistent with the vascular origin of tabes, the theory must be abandoned, no matter how plausible the laboratory arguments in its favour may be. But if the search-light of a wide clinical experience reveals no incidents in the history of the disease which are not more readily explicable upon this theory than upon any other, then the last convincing argument will be supplied in support of this truth. It is my opinion that the accurate clinical records of tabes will strengthen and not invalidate the above results of microscopical investigation.

The following case, which came under my observation, is full of interest. The main points to which I would draw attention are the state of the blood and the digestive tract, and especially to the diminished power of the latter to resist toxic substances.

W. B., aged 54, seaman, admitted to the poorhouse hospital in May, 1900, after an illness of over two years' duration, nearly half of which time had been spent in the wards of the Royal Infirmary, Edinburgh. His previous illnesses included small-pox (mild) as a child, malaria twenty years ago on the West Coast of Africa, dysentery on several occasions, "inflammation of the bowels" in Italy, and gonorrhoea. There was no history of syphilis. His present illness commenced about three years ago with severe vomiting, pain, and diarrhoea, which continued intermittently for a year, gradually becoming worse. About the same time frontal headache set in, limited to the left fronto-parietal side. This headache was usually associated with the gastric attacks, but was and is still frequently experienced independently in minor degrees. At the end of twelve months the diarrhoea gave place to constipation, the patient at this time having no passage for nine days. He was now admitted to the Royal Infirmary. He remained for three weeks in one of the medical wards without any improvement taking place in his condition. He was then sent to one of the surgical wards for operative treatment, a diagnosis of cancer of the stomach having been made. Operation was deferred, and he was again placed under medical care, but without benefit. About this time a tooth was extracted. This operation was followed by some necrosis of the jaw and a long-continued septic process, for which he was under surgical treatment for three months. The degree of local abscess formation necessitated external incision as well as active treatment inside the mouth. He was later sent to the Convalescent Home. For a time the pain and vomiting disappeared, and in October, 1899, months after the initial symptoms developed, he went back to sea. On the voyage he could not keep his feet, staggered much in his gait, and had difficulty in lifting his legs over the hatchway, and in holding on to the gangway ladder. The voyage lasted three weeks, after which he was readmitted to the Royal Infirmary. The diagnosis made in both wards was "tabes with amyotrophic changes." He continued to undergo slow deterioration and after a time was transferred to the poorhouse hospital. He now presents the characteristic picture of tabes dorsalis, namely, the loss of knee-jerks, lightning pains, ataxia, pupillary symptom, and gastric crises. He further exhibits symptoms indicating that the lesion is a widespread one, namely, a marked degree of motor weakness in the arms and legs, muscular atrophy, alteration in speech, and an altered mental state.

Since his admission to the poorhouse in May, 1900, he has had four typical and severe gastric crises. Each of these attacks has left him

worse than before. Prior to their occurrence there were indications of derangement of the digestive tract, distaste for food, discomfort, and increased fetor of dejecta. On inquiry we learn from his attendant that ever since his admission to the poorhouse the motions have from time to time been of a black tarry nature. This condition of stools occurs quite independently of the gastric crisis, which is associated with considerable hæmatemesis at the height of the attack.

The facts to which I would draw special attention in the foregoing are the following:

1. The previous illnesses of the patient afford good grounds for thinking that his general powers of resistance to all toxic agents might be materially lowered. This is especially true of the digestive tract.

2. His life and dietetic habits were specially favourable to a progressive diminution of the natural powers of resistance in the gastro-intestinal mucous membrane. I am, of course, aware that his habits would react unfavourably on all his tissues, including the nervous, but I believe that the primary mischief is of the local origin just indicated.

3. The initial symptoms, extending over a year, were directly referable to the digestive tract.

4. As a striking proof of the lowered power of resistance to toxic influences in the course of the disease, we have the long-continued suppuration and associated sapræmia already described. The readiness with which these patients succumb to an acute pyogenic invasion, cystitis, bronchitis, etc., in the later stages of the disease is of course well known, but it would be interesting to have statistical records of cases like the above, with the view of demonstrating the degree of lowered resisting power in the early stages of the disease.

5. The present state of the patient—namely, the continued fetor of the stools and melæna in the intervals between the paroxysms, indicates the importance of the intestinal lesions. Are these lesions of secondary or primary importance? I incline to the latter view.

6. The state of the blood. If my views as to the toxic origin of the disease are correct, I should expect to find certain changes in the blood, and it appeared to me advisable to investigate the point. Cabot in his recent work states that in locomotor ataxia the blood is normal. In the absence of any reference to a particular phase of the disease, I presume that he there refers to the blood in the interparoxysmal period of the disease. I am not aware of any observations having been made during the gastric or other crisis, although these are the points which demand special study. I took films from the case just recorded during the gastric crisis, and submitted them to Dr. Lovell Gulland, who kindly gave me the following report:

"Reds" seem to be normal, a few slightly altered in shape, but not more than the normal limit.

"Whites": If reds are normal in number, whites slightly increased, and the proportions of the different varieties point to a pathological leucocytosis.

Polymorph.	...	...	...	...	88 per cent.
Lymphocytes	...	...	...	...	11 per cent.
Eosinophiles	...	...	...	...	1 per cent.

No other abnormality in the leucocytes. Blood plates normal in number or slightly diminished. No organisms, blood parasites, or other abnormality observed.

This report suggests the advisability of a thorough investigation of the blood before, during, and after a crisis. The enumeration of the blood, and careful examination of stained films every four hours, might give us valuable information as to the degree of toxic action and the reaction of the tissues to its influence. I think it possible that the crises are of a nature akin to relapses in some recognised infective conditions.

The interesting question arises whether this case differs essentially from the less severe type of the disease with which we are more familiar, or whether the difference is merely one of degree. I incline to accept the latter view. It is interesting to note that another tabetic patient at present in the poorhouse hospital also exhibits from time to time marked intestinal symptoms (melæna, etc.). His stools, like that of the first case, are characterised by very marked persistent fetor.

When we come to consider the large and important group of cases commonly classed as anomalous, we find, I think, that their characteristic features are most readily explained in accordance with the vascular theory of the origin of the disease. Take the case reported by Buzzard in *Brain*, vol. i. 1878, under the title Amaurosis, Lightning Pains, Recurrent Herpes, no Ataxia. The attacks of pain and herpes appeared to the patient to be associated more or less with intestinal

disturbance. His feeling corresponds with the observation of Gowers, who has pointed out that lightning pains often accompany indigestion or constipation, and cease after an aperient has acted. If the theory of a general toxæmia with the alimentary canal as its chief source is valid, it is possible to explain the absence of severe symptoms from this case by the unusual degree of reaction in the digestive tract. Cases of a similar nature are, I believe, relatively common, and in all probability are merely examples of a more equal contest between the tissues and the toxin than obtains in cases where the disease runs a more rapid and severe course. This view gains in strength from the recently-expressed opinion of Babinski: "I believe I do not exaggerate when I say that in my hospital practice I see from 200 to 300 cases of tabes each year, and of this number I do not see more than 15 to 20 who are clearly ataxic subjects. In my private practice I have numerous patients who have been for many years affected with tabes as judged by its characteristic signs, and who, without retaining an absolutely perfect form of co-ordination, have continued at their usual employments and have never passed the so-called preataxic stage."

Again, what theory will so readily explain the various transient paralyses that are such a conspicuous feature of the disease? These represent merely incidents in the general toxæmia and are, I think, best understood by reference to local resistance in the area supplied by the vessels involved, and by a relative acquired immunity. They should, in fact, be brought into line with the comparative cases previously referred to.

The vascular theory would also help to explain the exact nature of the relationship which the onset of the disease bears in some cases to traumatism, exposure to cold and the like, and in a similar way it would bring fresh light to bear on other questions that have from time to time arisen, for example, the existence of a causal relationship between tabes and heart lesions. When this relation was first observed, its explanation was attempted along "nervous" lines, that is to say, the heart condition was supposed to be dependent on the results of some interference with its nervous mechanism analogous to the changes in other parts of the nervous system, a view which has rightly fallen into disrepute. In its place we have the present view—that the cardiac lesions are of syphilitic origin. This explanation assumes that heart complications will not arise in cases of tabes in which a syphilitic history cannot be traced. I believe that if the condition be looked at from the point of view of a general toxæmia, which may occur quite independently of syphilis, a more adequate explanation will be provided.

Then, again, does not the vascular theory account better for such conditions as tabetic ecchymosis, and also for the great variety of clinical features seen especially in advanced cases, for example, the frequent association of paresis, muscular atrophy, etc., pointing to the involvement of regions of the cord, which have no direct anatomical or physiological continuity with the part most affected? But perhaps the best instance of the elucidating power of the vascular theory will be found in the light thrown upon the occurrence of those apoplectic attacks which, in their slighter forms, are so frequent in the course of the disease. Such hæmorrhages (and thromboses also) are already known to be the result of the long-continued presence of some toxic agent, and of its action, not, be it noted, on the neurons supplied by these vessels, but on the vessels themselves. The important examples which I have just given of incidental features in tabetic subjects indicate that we need not expect a serious challenge of the vascular theory from the standpoint of clinical experience.

MENTAL SYMPTOMS IN TABES.

I have under my observation at present four cases of tabes, in all of which distinct symptoms of mental enfeeblement and perversion are present. In two cases the symptoms are very pronounced, yet none of the four conform to the classical description of general paralysis. There is a tendency at present to associate tabes and general paralysis so closely that we are in danger of ignoring the broad fact that tabes is a general disease liable to be accompanied by mental symptoms, which differ in type and severity according to the principles of individual reaction. In many cases the resulting picture does not conform to the recognised description of general para-

lysis. If our general argument is correct, the field of tabes must include not only those nondescript cases but also such variants of nervous disorder as Friedreich's ataxia.

There now remain, according to the scope of this paper, only two questions to be answered. First, how does the theory of vascular origin consist with the varying degrees of degeneration in the different columns?

Limits of space will only permit me to indicate the appropriate lines of reply. In the first place, the condition referred to is not confined to tabes. There are a large number of diseases, notably diabetes, pernicious anæmia, ergotism, pellagra, senile and malignant cachexia, intracranial tumours, etc., in which recent investigations have disclosed lesions of the cord, most marked in the posterior columns. A description of the various conditions will be found in the *Archives de Neurologie* of December, 1900, and January, 1901, which contain a summary of the discussion on these subjects at the Paris Congress. When we consider the wide diversity of these diseases, not only from tabes but from each other, we are compelled to see in the similarity of the resultant condition a distinct argument in favour of the vascular origin of tabes. At the very least, we are precluded from regarding the neuron as of primary, and the vessels as of secondary, importance, unless we are prepared, on account of the condition of the cord, to place these heterogeneous disorders in a single class of "nervous" diseases.

In the second place, if we leave tabes out of consideration, the histological examination of the cord in these other diseases is sufficient to establish the truth of the general statement that the posterior part of the cord is naturally more susceptible than the rest to the action of toxic agents. This greater susceptibility is, as a rule, most readily observed in the lumbar cord, and the explanation naturally suggests itself that this is due to the relatively greater blood supply. No difficulty therefore arises from the different degrees of degeneration in the cord. On the contrary, it is seen that the adoption of the vascular theory would effect a most important simplification in pathology.

In the third place, so far is the vascular theory from being inconsistent with varying degrees of degeneration in different regions of the cord, that I believe it would present no difficulty if the degeneration were entirely confined to the posterior columns. Just as in general paralysis one set of vessels in the cortex is mainly affected through the selective action of the toxic agent, so in tabes there is a selective action on the vessels of the posterior columns.

The second and last question which calls for answer is, What effect would the establishment of the vascular theory have upon the prevailing opinion that tabes has a syphilitic origin?

At present three distinct positions are taken up regarding the existence of a causal relation between syphilis and tabes. The position of extreme affirmation is occupied by Ferrier and others, whose opinion may be briefly expressed in the brocard "No syphilis, no tabes." At the other extreme stand Leyden and others, who either deny the relation altogether, or hold that it is still unproved. A middle position is assumed by the great majority of investigators, who maintain that 60 to 90 per cent. of the cases of tabes are due to syphilis. But since the disease, unlike the well-recognised syphilitic lesions, does not yield to antisyphilitic treatment, it is admitted that the relationship is more complex than in other syphilitic affections. The nature of this modified relation has been described by such terms as "parasymphilitic," "post-symphilitic," etc. Underlying the use of these terms and the classification they effect, there is, it seems to me, an important fallacy. It is customary in writings on the etiology of chronic nerve affections to place syphilis, lead, alcohol, etc., together in a group of causes. It is thereby implied that the morbid agency of syphilis, itself a disease, is on a par with the action of such poisons. Surely that is not so. In the case of a toxic substance of a known chemical nature, such as lead, we are dealing with certain doses over a long period, the tissues having considerable opportunities for readjusting themselves so as to secure relative immunity. In syphilis the case is quite distinct. We are there dealing with the sum total of individual reaction to the syphilitic virus from the definite moment of its introduction up to the time at which the patient comes under observation. Apart

from this, I maintain that the syphilitic origin of tabes is a mere *non sequitur* from the fact that a syphilitic history can be traced in a large number of tabetic subjects. In strict logic, the broadest conclusion which we can deduce from that fact is that syphilis alters the physiological condition in such a way as to favour the attack and operation of the actual cause of tabes and allied conditions. In this respect its influence, in my opinion, is similar to that of measles or scarlet fever in leading to the development of tuberculosis, and similar also to the action of the influenza bacillus in relation to other pathogenic organisms.

When to these facts of clinical experience we add the evidence of experimental bacteriology, from which we learn, for example, that the presence of staphylococci and streptococci leads to a much more luxuriant growth of the influenza bacillus, and further, that the latter will grow more readily in a medium through which these other organisms have passed, we are strongly attracted to the existence of an analogy in the relation of the syphilitic virus to the toxic agent responsible for tabes.

I submit that the proper line of investigation is directed to the discovery of the nature and source of the toxic substance at work. At the same time we must study the clinical facts of the disease in the light of the results obtained by experimental bacteriologists and others investigating the all-important subject of immunity. In my opinion the alimentary tract furnishes the chief area of investigation, and in all probability it will be proved to be the original source of the toxæmia. In this connection it is interesting to refer to the experimental work of Adami and others on the different forms of chronic infection due primarily to the presence in the tissues of bacterial poisons derived from the intestine. The diseases specially investigated by Adami were cirrhosis of the liver, hæmochromatosis, and pernicious anæmia, and this author, as quoted by Putnam and Taylor,⁸ suggested that this subinfection would be found to play a definite part in the development of many chronic fibroid conditions.

In conclusion, I have much pleasure in expressing my indebtedness to Dr. Ford Robertson, Director of the Laboratory of the Scottish Asylums, for invaluable assistance. It was originally proposed that a joint communication should be written by us, but the pressure of other work compelled Dr. Robertson to abandon the idea. He has, however, kindly allowed me to state that he accepts the interpretation which I have put on the histological appearances described. I have also to thank Dr. Carmichael for permission to investigate and record the cases of tabes under his care in the poorhouse hospital; Dr. W. R. Watson, Hawkhead Asylum, Paisley, for the tissues from which most of the illustrations have been derived; and the various members of the staff of the Royal Infirmary, who have kindly given me material used in the course of the investigation.

NOTE AND REFERENCES.

¹ *Arch. de Neurol.*, January, 1901. ² A histological demonstration of the condition of the cord was given to the Medico-Chirurgical Society some months ago, and the case has been fully recorded in the *Veterinary Journal*, March, 1901. ³ *Veterinary Journal*, June, 1901. ⁴ *Pathological Anatomy of a Case of Tabes with General Paralysis*, *Brain*, vol. xii. ⁵ *Brain*, vol. v. ⁶ *Neurol. Centralbl.*, vol. iv. ⁷ *Archives de Neurologie*, December, 1900, Discussion, p. 507. ⁸ *Jour. of Nerv. and Ment. Dis.*, January and February, 1901.

CASE OF MALIGNANT DISEASE OF THE LUNG, WITH PSEUDO-TUBERCULOSIS.

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THE literature dealing with the double infection of lung tissue by cancer or sarcoma and the tubercle bacilli is necessarily limited to the description of cases since 1882. It is, however, very remarkable how few cases have been described in which active tuberculosis of the lungs has been met with in association with cancer or sarcoma of the same organ.

History.—A gasfitter, aged 27, was admitted to University College Hospital suffering from pain in the left side of the chest, shortness of breath, and weakness. These symptoms had been present for four months, coming on rather suddenly in an attack of what was considered to be influenza; ultimately "pneumonia and pleurisy" developed.

State on Examination.—On admission the patient looked very ill, was distressed in breathing, and had a short spasmodic cough, which caused considerable pain in the left chest, and was accompanied by a copious

frothy expectoration. The left chest moved less than the right, and there was considerable flattening at the left apex, and on the same side the vocal fremitus was weak and the percussion note in the lower part of the axilla was dull, though a skodaic note was obtained at the apex. The breath sounds on the left side were very weak, more especially at the base. The temperature was 103.4°, pulse 100, and respiration frequency 36. Fluid was suspected at the left base, and a needle was inserted, but with negative results.

Progress.—Results. Nine days later the sputum became purulent, though very tenacious as on admission. Throughout the illness the temperature was raised, varying from 100° to 103°, the pulse increased to 120 per minute, the respiration to 40. Fifteen days after admission the patient's condition suddenly became much worse; he coughed up about half a pint of very offensive purulent material and had great dyspnoea and cyanosis. The earlier diagnosis of left pleural effusion having been disproved, and these acute symptoms appearing, it was thought an abscess or tuberculous cavity had suddenly burst into a bronchial tube or an empyema had burst into the lung, so a trochar was again inserted into the left base and a few drachms of blood-stained offensive pus were drawn off; the patient's strength, however, was falling so much that it was thought inadvisable to reset a portion of a rib. The patient died a few hours later.

Necropsy.—A round-celled sarcoma was found involving the root of the left lung constricting the vessels and bronchus; the apex of the left lung was somewhat consolidated, and showed numerous granulations resembling tuberculous granulomata (see photographs); the upper lobe of the lung was also the seat of an infarction. The middle and lower portions of the lower lobe were in part riddled with cavities, in some cases large enough to admit a walnut; in part the lung was consolidated, and showed, especially at the base, yellowish-white areas, in some cases quite caseous. Signs of antecedent and recent pleurisy were present in the left lung. The cavities above mentioned contained offensive greenish pus. The naked-eye appearances suggested at once that the sarcoma, by pressing on the bronchus and vessels, had so interfered with the lung that tubercle bacilli had developed over a considerable part of the lower lobe, producing a pneumonic condition with cavities, and had begun to invade the apex of the lung. The right lung was quite free from disease. Microscopic examination was made of the left lung; sections were made of the granulations at the apex, of the pneumonic areas present at the base, and of the walls of the abscess cavities, and Ziehl-Neelsen's method applied for the detection of tubercle bacilli, but with negative results. Film preparations were made of the contents of the cavities, and again tubercle bacilli were not found. No inoculation experiments were made, as the specimen had been kept in formalin for some time before the microscopic examination had been made. Some twenty-five or thirty preparations were made altogether, and in nearly all of them streptococci, staphylococci and a few slender bacilli were found. No giant cells were seen or tuberculous granuloma systems, but abundant fibrinous exudation was seen in many of the alveoli. The granulations above mentioned proved to be mere foci of fibrinous pneumonia.

The pathological diagnosis thus resolved itself into one of sarcoma of the root of the left lung, producing stenosis of the bronchus and vessels, and associated with pneumonia of the lung, probably due to the septic organisms present. The lung condition so closely resembled that met with in tuberculosis, with the exception that the process was more marked at the base than the apex, as to merit the application of the term pseudo-tuberculosis. In accordance with the report of a subcommittee on pseudo-tuberculosis in 1899, appointed by the Pathological Society, such a term is inadmissible, and the granulations found in the lung alone had better be described as "coccal" or "bacillary" nodules.

Though modern research has shown that all cases of granulomatous disease in which the granulomata closely resemble the tuberculous granulomata, are not necessarily due to the tubercle bacillus, so that observers working before 1882 may have misnamed many pathological specimens, it is very striking how comparatively rare is the infection of the body or particular organs with tuberculous disease and cancer or sarcoma. Walshe¹ and Rokitsky,² writing in 1846, were both impressed by this observation. Rokitsky admitted that cancer followed tuberculous disease, and rarely tuberculosis followed cancer; in either case the combination was not frequently met with. Walshe found in 104 cases drawn from his own personal experience or from reliable sources, only 7 cases of malignant and tuberculous disease of the lung occurring at the same time. Walshe quotes Bayle, who found the same combination in 3 cases out of 900 cases of phthisis. Pollock³ described a case of mediastinal growth of the right lung complicated by tuberculous deposits at the apex of the lung on the same side. No cavities were present, but Quain, who examined the specimen, confirmed Pollock's opinion that the granulations were tuberculous, and found large cells present, containing several nuclei.

Bristowe⁴ described another case showing miliary tubercles at the apex of the left lung also in the right lung, and consolidation and cavities were also seen; a cancerous growth involved the root of the right lung and a secondary deposit was present in the liver. Bristowe thought the granulomata were tuberculous, but Jenner and Brinton were convinced that the