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The Morison Lectures

ON

**NERVOUS SEMEIOLOGY, WITH SPECIAL
REFERENCE TO EPILEPSY.**

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BY

S. A. KINNIER WILSON, M.D., F.R.C.P.,

NEUROLOGIST AND LECTURER IN NEUROLOGY, KING'S COLLEGE HOSPITAL.

**LECTURE I.—THE RELATION OF NERVOUS
SYMPTOMS TO NERVOUS LESIONS.**

It is my first and pleasing duty to express to the President and Council of the Royal College of Physicians of Edinburgh my deep appreciation of the signal honour paid me by the request to deliver the Morison Lectures. Scanning the list of my distinguished predecessors and the subjects chosen by them, I find that comparatively few have in recent years dealt with any special aspect of neurology, and I am glad to take this chance of submitting to the consideration of my confreres some matters bearing on nervous semeiology and on the interrelation of nervous symptoms and lesions to which I have long given thought. I do this with no little diffidence, however, because the general considerations to the importance of which I have become increasingly attached will doubtless appear to a number familiar and possibly axiomatic; yet they may prove not without interest as representing, in some degree, certain changes in my own views on fundamental problems of interpretation that concern every neurologist. There is also advantage in allowing oneself the leisure for a look round, seeing that the directional flow of a stream is not always appreciated by those whose attention is centred on eddies, pools, or backwaters.

As a tyro in the subject of nervous diseases I imagine I began with a conception based on clinical differentia; it seemed practical enough to separate cases in accordance with their particular semeiology; a given disease was represented clinically by a corresponding syndrome or symptom-complex, and even if specific modifications were found the generic picture could always be relied on for purposes of diagnosis. The typical syndrome of disseminated sclerosis was constituted by the old Charcotian triad of intention tremor, nystagmus, and scanning speech; that of tabes by Argyll Robertson pupil, lightning pains, ataxia, and loss of deep reflexes; of infantile paralysis by flaccid palsies, wasted muscles, and deformities; and so forth. Yet it did not take long to be convinced of the limitations of a purely clinical arrangement, for the fact was soon discovered that one and the same symptom can arise in conjunction with lesions at different physiological levels in the nervous system, and as a result of different pathogenic actions. Besides, experience showed the futility of the endeavour to circumscribe the clinical tableau of a given affection by a series of Procrustean lops. Epidemic encephalitis may be thought by some to be one and indivisible, but so far as its semeiology is concerned its manifestations are legion.

The next step, under the influence of honoured teachers of twenty-five years ago, was to rely on the well-tried clinico-anatomical method, to correlate symptoms during life with lesions found after death, and to assume (if not always to demonstrate) their essential consonance. I am

the last person to decry the value of the method in its time, for there can be no doubt, in the first place, that such correlation (with certain provisos) is legitimate enough, and in the second, that its employment has led to discoveries and advances of the first importance. Indeed, I suppose the devotees of what has been called the necrological school of medical thought are as numerous as ever, and will continue to be reinforced by successive generations of medical students unless and until their preceptors are sufficiently emboldened to point out its rather misleading assumptions. The method, if I mistake not, is becoming just a little *démodé*, although years have already elapsed since that shrewd observer the late Sir James Goodhart wrote a paper on "The passing of morbid anatomy," which exercised more than a transient influence on my own views. Hopeful lines of present-day research are directed to study of the living in preference to scrutiny of the dead, and some day diagnostic autopsies will be a reproach and not a satisfaction.

It appears to me incontrovertible that neither a clinical nor a pathological classification offers any particular advantage from the standpoint of nosology, and that the sole basis for the scientific arrangement of nervous disease is etiology. Yet this is precisely the department of investigation which lags behind. The causation of a large group of nervous affections is undiscovered, but until we find initiating factors we dare not begin to speak of such and such a clinico-pathological combination as constituting a disease. The day has passed for the physician to transform clinical syndromes and pathological complexes into diseases. For what is a disease? Obviously, it is neither the etiological excitant, nor the clinical *allure*, nor any underlying pathological change; and we may with Sir Humphry Rolleston allege that it is nothing else than a mental picture—a conception figured in the mind, a composite of elements no one of which by itself suffices to define. At any rate, we shall find great, nay, insuperable, difficulty in establishing disease entities unless we can prove that a given causative agent produces invariably and solely the same reaction in the body, exhibiting the same syndromes, and amenable to the same treatment.

THE PHYSIOLOGICAL NATURE OF SYMPTOMS.

1. It will, I think, be generally allowed that an etiological factor, a pathogenic agent, can be regarded physiologically as a stimulus, and physiology recognizes only three classes of stimuli—namely, pure excitants, pure depressants, and those which first excite and then depress. Accordingly, clinical symptoms are to be considered as representing either excitation or cessation of function, or a series in which the latter follows the former. Without exception, all are functional, in the sense of being related to function. To attempt to distinguish "functional" from "organic" symptoms is therefore meaningless. This, so far as I personally am concerned, is an ancient platitude; I date my awakening to a conversation with my old teacher, the late Dr. Charlton Bastian, who, when I told him a patient had been admitted under his care suffering from what I, with the dogmatism of the house-physician, described as "functional fits," replied: "Did you ever see a fit that was not functional?" I then secured an insight into semeiology which I trust I have never since failed to maintain. Whether we deal with motor, sensory, vegetative, or psychical symptoms, each and all are classifiable as consisting of either increase (inclusive of "escape") of function, or of decrease, and there is nothing else.

2. A symptom is the expression of a physiological reaction, and hence can never be specific unless we imagine

reactions themselves to be so—an impossibility when the unbelievable diversity of stimuli is born in mind. Take any banal symptom of neurology—headache, neuralgia, hemiplegia, paraplegia, amyotrophy, anaesthesia—everyone recognizes their production by a host of differing agencies. With advance of knowledge the alleged specificity of many a neurological symptom is steadily undermined, till we may well question whether any at all can thus be distinguished. An Argyll Robertson pupil is just as characteristic of collicular neoplasm as of neurosyphilis; the epileptic fit occurs as a semeiological incident in circumstances we should never dream of ascribing to a “disease” called “epilepsy”; intention-tremor is by no means confined to the subjects of disseminated sclerosis. I have not myself seen a case of rabies; but no one who is conversant with the graphic descriptions of older observers can fail to notice either the remarkable similarity of recorded cases as regards the dramatic consequences of any attempt to swallow fluids, or the overwhelming consensus of opinion that such symptoms are so pathognomonic of the disease as to provide it with one of its names. Here, however, is a recent account, reported by Fletcher and Fitzpatrick¹ in the *Lancet* of 1927.

“When he attempted to swallow the result was terrible. While we were examining him he asked for some iced water, but no sooner did he put the cup to his lips than he was seized with violent spasms of the throat, jaws, and left side of his face. The small amount of fluid which had entered his mouth was shot out again with a hissing sound; short, sharp hisses followed each other at intervals of about half a second. With each hiss the head was jerked forward by a spasm of the sterno-mastoids, and sometimes the hiss ended in a sharp sound like a bark. The patient must have remained in this torture for a minute or more,” etc.

No feature of the spasms of hydrophobia is wanting, not even the bark; the case, however, was one of tetanus. Further comment would surely be superfluous.

3. Being the expression of a process (of excitation or depression, as the case may be) a symptom is likely to be fluctuating and variable; it may wax and wane, rise and fall; it need not be the same at each examination, and therefore any argument that “organic” can be differentiated from “functional” symptoms by their relatively unchanging character, or their persistent nature, or their being uninfluenced by factors of a different order, is at once vitiated. The tremor of paralysis agitans is as patently under the influence of emotional and other psychical stimuli as is that of hysteria; it may be present at one moment and absent the next (an observation made originally by James Parkinson² himself). A number of illustrations of this clinical fact were given in the Croonian Lectures³ of 1925. Similarly, in cases of progressive lenticular degeneration I have had occasion to observe the remarkable “fluidity” of the tremor, which may leave one group for no apparent reason to develop forthwith in some other, separate, distribution. The tremor of hysteria, in point of fact, does not often itself exhibit such variability. Only when a structural change is permanent, when tissue reaction has come to an end, does a given symptom become stabilized or static. In itself it stands in no constant relationship whatever to underlying structural alterations. Thus may we observe a patient with disseminated sclerosis exhibiting ankle clonus one week and none the next; but even more illustrative instances are at hand. In the course of the cataplectic attack of narcolepsy the knee-jerks are abolished as completely, as “organically,” as in a case of tabes with sclerosis of dorsal columns—yet only for a few seconds or minutes. One of my narcoleptic patients at hospital, a girl of 18, fell sound asleep in the ophthalmic room after I had been looking at her discs; during this sleep tapping her patellar tendons yielded one single, brief, and faint twitch, and thereafter they were totally irresponsive to repeated percussion; yet when she awoke, walked into another room, and sat down, the knee-jerks were found again to be brisk. Recent work by Jacobson⁴ in the University of Chicago has proved that a normal subject may so relax himself voluntarily, may empty his muscles of tone to such a degree, that in the course of a few minutes the knee-jerks may be

entirely abolished. I had occasion to sit by the bedside of an old gentleman of 70, who complained of recurring attacks of right-sided weakness; on my first examination he showed neither symptom nor sign of abnormality, but while I was talking to him he suddenly remarked, “It’s coming back now,” and a minute later he could move neither arm nor leg. I then found a characteristic extensor plantar response where a moment before it had been flexor, and the abdominal reflex disappeared. Ten minutes later, power returned, and once more the plantar reaction was in flexion.

From these and numerous examples that come to mind, which can surely be paralleled in the experience of most neurologists, I submit only one conclusion can be drawn—namely, that symptoms *per se* are the expression of dynamic alterations in function, and either may or may not coincide with structural change. To ascribe of necessity to structural lesions what we have been in the habit of thinking “organic” signs is therefore improper; only when the latter are residual and static is it legitimate to attribute to them such clinical phenomena. Otherwise, indeed, our talk of “recovery of function” is meaningless. A further conclusion is, that in themselves it is impossible to differentiate between symptoms due to dynamic and to static change; an extensor response which is present for five minutes, a knee-jerk which is absent for the same time, are indistinguishable from those that endure.

DEFECTS OF THE CLINICO-ANATOMICAL METHOD.

When we endeavour to link the clinical symptoms of illness with any tissue modifications found subsequently, our path is beset with pitfalls of a sufficiently obvious kind.

1. In the first place, we have to consider the precise nature of the semeiological picture during life. Adopting Jacksonian terminology, we must state whether the symptoms are “positive” or “negative”—that is, whether they correspond to enhanced or diminished function, to its presence or absence. Clearly, excitation of function cannot be associated with destructive lesions; the sole direct effect of the latter must be its abolition. When we find paralyzes or anaesthesias or amyotrophies, we can properly assign them to interruption or disintegration of nervous tissues. But it is far otherwise with “positive” symptoms, of which a moment’s thought will convince the clinician a large part of nervous semeiology is composed. These must be produced by the action of healthy mechanisms. To attribute the involuntary flexor spasms of a case of paraplegia to lesions in the pyramidal tract is illogical; for their occurrence integrity of lower spinal reflex arcs is essential. That is to say, a prominent symptom is produced by the action of a healthy mechanism. The problem of all involuntary movements (tics, chorea, tremor, epilepsy, myoclonus, athetosis, etc.) is a problem in physiology, and will never be solved by their ascription to destroyed cell-fibre systems. Or take another example: in the case of neuralgia, precisely what lesion do we expect to discover that can be correlated with it? Essentially a positive symptom, it must be caused by excitation (or release, if that is thought more accurate physiologically) of sensory mechanisms which must be in a state of health, not of depression. Can such cell-fibre systems be distinguished histologically from any others? What can we suppose is the state of the dorsal root ganglia in the persistent pains of tabes? Logic insists that a neurone or neurones responsible for the conveyance and experience in consciousness of impulses underlying pain must be histologically intact, and not in a condition of degeneration. To find such ganglia indistinguishable from any of the rest, so far as the cells are concerned, would be in no way surprising, but quite the reverse.

This provides, indeed, a sufficiently plausible reason for postulating a sensory inhibiting system of *efferent* type, as has been advanced by Foerster⁵ and others, both before him and since; the suggestion then would be that de-inhibition of this system by destroying agencies would allow overaction on the afferent sensory system whereby pain (for instance) would be persistently experienced in consciousness.

What changes is it rational to expect in the spinal cord of a patient who has suffered from tetanus—I mean in

relation to his clinical symptoms? Not a few modern cases are on record (cf. Aschoff and Reinhold⁶) with either minimal cellular change or indeed with none that is recognizable. So far from this situation proving disconcerting, it is, I submit, entirely the other way. The purer the action of tetanus bacilli and toxins—that is to say, the less the histological picture is complicated by antitoxin, magnesium sulphate, or narcotic treatment during life—the more insignificant are the departures from cellular normality. If a patient dies from the affection we surely cannot expect to discover identical modifications in the cells whose activity has been responsible for tetanic spasms, and in those whose paralysis has caused death. In respect of the former we should postulate, and expect to find, integrity and not disease. Logically, once more, we should be unable to correlate a pronounced symptom with any lesion of the mechanisms producing it.

2. No constant relationship holds between size of lesion and amount of functional disorder. In a given case the most prominent clinical symptoms are by no means necessarily coupled with the lesions most apparent at the *sectio*. The widespread functional disturbance of a generalized major epileptic seizure, which ranges, in fact, from hallucination to micturition, stands in no proportionate relation whatever to any "lesion" that may subsequently be demonstrated. No connexion exists between the mass of a cerebral tumour and its symptomatology; some, for that matter, are discovered only after death. For the immense range of symptoms badly classed as "subjective" no objective basis is supposed to exist—though, of course, we know they must have a physiology.

3. The localization of a symptom, a functional system, and a lesion, is in each instance a different and separate thing; and herein lies one of the more serious shortcomings of the clinico-anatomical method. A capsular haemorrhage produces a paralytic hemiplegia; but any inference that motor function is confined to the pyramidal system is clearly erroneous. Its substratum extends far beyond that part a lesion of which is followed by motor symptoms of a negative kind. When the contracted fingers of the hemiplegic hand open in extension as the patient yawns the symptom (an involuntary movement) has nothing to do, *qua* localization, with a thrombosis on the pyramidal path. The phenomenon of micrographia doubtless is a symptom of some cases of Parkinsonism, post-encephalitic or otherwise, but it is also found in cerebral arteriopathies, in hemiplegics, and in normal subjects. How, then, in the name of all that is logical, can it be "localized" in the corpus striatum, as some would maintain? The same considerations hold good in respect of the sensory system; we "refer" or "localize" sensory symptoms to or in various parts of the body, whereas, as a fact, every sensation is a presentation in consciousness, and therefore of, let us say, cortical site. Yet the lesion stands in no spatial relation thereto. Central pains arise in association with a lesion which may be situated in spinal cord, pons, or thalamus; but, whatever its position, it cannot correspond to the place where sensation is being experienced.

Symptoms, lesions, and functional systems are not comparable, cannot be, as it were, superimposed one on the other, and obey differing rules of localization. It would be a simple matter to amplify the contention by a further series of illustrations, but one must suffice. For a number of years many writers, more especially on the Continent, have been assigning post-encephalitic tics to destructive lesions of the putamen or caudate nucleus. Now such a view can be shown to be doubly or triply erroneous; for in the first place a tic is a positive movement and must be caused by activity of motor cells; it cannot be assigned to those that are dead. Secondly, it represents a mode of activity of the motor system, and as such its intrinsic clinical characters compel us to place it at a high level in that system, certainly not at an infracortical site. Thirdly, it exemplifies escape of motor function from control, and if a lesion is to be sought therefor, that lesion may be situated in transcortical inhibitory mechanisms far removed anatomically from the region whose healthy activity is causing the tic. No adequate reason perhaps exists for seeking any recognizable lesion for habitual movements, tricks of motor type, mannerisms, stereotypies; if there be any at all, it

is one which is responsible for de-control only, and unfortunately we do not know what and where that may be; we postulate transcortical defect without being able to specify it.

There is, however, a still more radical objection to the mode of thinking which associates physiological symptoms with visible lesions. We must, I believe, definitely concede that in respect of the motor system (say, the motor region of the cortex) excitation can produce immediately obvious motor symptoms, whereas limited destructive lesions of the same part may not cause any paralysis. Movements are represented over relatively wide areas, and unless the part destroyed is sufficiently large it may not effect any interference with movement production. Thus small lesions in cerebellum, corpus striatum, or cortex itself may not be responsible for any discoverable symptom if the function or functions concerned enjoy a wide representation. To link a lesion of such a kind, therefore, with the active manifestation of a movement is an unsound and indefensible proceeding. I am tempted to add another corroboration of the general argument of value because it concerns a negative symptom—namely, agraphia. For my present purpose the term may be taken to signify inability to write correctly as regards formation of letters and words. Say that this occurs in consequence of a stroke with right hemiplegia in a right-handed person. Assume that his incapacity is not so severe as to prevent his holding the pencil properly enough, and that he has preserved in his mind the necessary ideas, but—he cannot write. To ascribe this symptom to a destructive lesion which may be found post mortem in the left hemisphere is facile, and the corollary is practically certain to be drawn that the area involved is a "writing centre." But surely here is a complete *non sequitur*. Have we tried our patient's left hand? If he can write with it, there is no agraphia at all. Have we thought of trying him with his toes? It is relatively easy to write with the foot if the pencil is suitably fixed, and in even more unexpected ways—for example, with the pen between the teeth. I have a pen-and-ink signature thus written solely by movements of the head, executed by a soldier with complete traumatic quadriplegia. Where, then, is the writing centre? At the least, it is not where a destroying lesion interferes with conduction to the right arm and hand. Did not Grock, the French clown, play the piano with his nose? And if a lesion were to obstruct the route from temporal lobe to neck muscles, would he suffer from amusia?

4. A further frequent misunderstanding in respect of clinico-anatomical correlation is concerned with the question of time. I know well, of course, that one lesion can often be shown to be older than another in the same brain, but this declaration is of minor significance compared with the inability of the neuropathologist to do more than present a static tissue-picture in contrast to what has consisted in life of a physiological progression, a series of functional events. The temptation is almost irresistible to set a pronounced clinical symptom alongside an obvious structural change without considering the approximate time of development of either. If yielded to, the result may be unfortunate. A striking example comes to mind. The average duration of a case of rabies is only three days if incubation occupies less than thirty, and only four when more than sixty—in either instance extremely brief. Some recent studies (cf. Schükri and Spatz⁷) have demonstrated conclusively that even without that short period of four days the substantia nigra is the most heavily implicated of all affected regions; many of its ganglion cells are totally disintegrated and glial scavenger cells packed full of melanotic pigment. This simple fact—namely, that degeneration and disappearance of the cells of that structure are seen in acute rabic cases well inside a week—at once renders extremely suspect any ascription of the Parkinsonian syndrome of epidemic encephalitis to their absence in that affection, since (apart from the definitely positive nature of the syndrome) it leaves out of account the fundamental question of the time factor. Should the objection be raised that the comparison is of two different morbid affections, I may point out that in epidemic encephalitis Greenfield⁸ has noted destruction of these cells by the twenty-third day. When Parkinsonism develops, say, two years after the acute attack, and at a *sectio* five years later outfall of the cellular

elements of the substantia nigra is apparent, how can we allege clinico-anatomical relationship if we do not know at what time they disappeared? Without such knowledge we are committing the easy error of setting in juxtaposition merely the obvious symptom and lesion and of ignoring the time component.

But there is another aspect of the same topic that merits attention. A syndrome whose unrolling involves the idea of succession in time cannot be localized by spatial rules. Discussing this point, Monakow and Mourgue⁹ take as illustration a musical box, in which dissonance can be produced (1) by absence of one or more projections on the rotating brass cylinder, (2) or absence of teeth in the vibrating comb, (3) or by changing the position of the latter in relation to the former to right or left. Incidentally, we have here a useful proof of the fact that one and the same symptom can be caused by changes at different physiological levels, as already remarked. All such possibilities effect alterations in temporal succession and modify the melody; but if the question is asked, "Where is the melody localized?" it is seen to have no meaning. Its "localization" is chronogenic. Some time ago neurologists were seeing cases of post-encephalitis characterized by inversion of sleep rhythm—a rather difficult symptom to deal with, and often extremely pronounced; the youthful patients were sleepy or asleep during the day, and became imps of mischief during the night. Here is a symptom, definite and special, but where is it localized? One has only to set the question to perceive its absurdity. And this leads naturally to the cognate question of narcoleptic phenomenology. In view of the fact that all of us sleep for a number of hours during the twenty-four, what exactly do we expect to find should such a case come to necropsy? I cannot see that occasional or even frequent diurnal sleeps are calculated to effect any persisting morphological change in nerve cells; and if none is recognizable what becomes of the relation of symptoms to lesions? It is perfectly clear that the narcoleptic patient is suffering from a derangement of sleep rhythm, a hypersomnia which is merely an exaggeration of a condition recurring normally in every one of us every day, and I submit that that disorder of the processes of sleep constitutes a symptom embodying the idea of modification in time and cannot be interpreted by reference simply to static change. Even if organic lesions are seen post mortem in a case characterized by pathological sleep—as occurs often enough—it behoves the neurologist to proceed warily in his correlation of the two. To explain alterations in time processes by morphological tissue change is strictly an illogical procedure.

We have thus seen how lesions can be present without recognizable symptoms, and symptoms without recognizable lesions. So far, however, from being nonplussed thereby, I am clearly of the opinion that not only is this to be expected, but that it also throws light on the true nature of what in a superficial way is termed "disease." Rather should any scientific parlance employ the term "reaction" as explanatory of symptom-lesion relationship; and it is informative to note that some present-day psychiatrists—dissatisfied with Kraepelinian conceptions—now speak of paranoid reaction types, schizophrenic reaction types, etc., instead of paranoia, schizophrenia, and so on, once thought to constitute actual disease entities.

INTERPRETATION OF NEUROPATHOLOGICAL CHANGE.

Since no specificity, as we have found, attaches in a general way to nervous symptoms, their causation being—again speaking generally—multiplex, the homologous question of whether pathological changes can be considered specific becomes of much interest. My submission is that they cannot so be regarded; that they are nothing else than tissue reactions to noxious agents; classifiable no doubt in certain groups, they form none the less merely a series of pictures, the features of any one of which are as a fact common to numerous others.

We may begin by looking for a moment at cellular change. Now Nissl himself, who at first hoped for and believed in an unvarying correspondence between specific poisons and specific cell alterations, was compelled in the

end to concede that similar or identical changes can be brought about by a whole series of etiologically distinct factors—an admission that must be fully accepted by everyone who has any knowledge of the subject. The statement of Dejerine,¹⁰ made as long ago as 1897, that "la chromatolyse de la cellule nerveuse est une lésion banale, intéressante au point de vue cytologique, mais jusqu'ici, du moins, ne répond à aucun phénomène physiologique et, partout, pathologique déterminé," is for practical purposes almost as true to-day as it was thirty years ago. I need scarcely point out, by way of illustration, that swelling of the nerve cell occurs in fevers, alcoholism, botulism, strychnine poisoning; diffuse coloration of the achromatic substance in diphtheria, lead and phosphorus poisoning, and various mental affections; vacuolation in toxicosis from cocaine, morphine, chloroform, and in such infections as rabies, cholera, plague; enlargement of the nucleus in burns, uraemia, cholaemia; nuclear shrinkage in poisoning by arsenic, alcohol, etc., and in eclampsia; nuclear displacement in pneumonia, typhus, morphinism, cocaineism; and so on and so forth. None of these reactions are mutually exclusive, none a feature of one class more than another.

Or take the mesodermal—that is, conjunctivo-vascular—reactions, considered nowadays to form the correlate of inflammation in the central nervous system. Here are included cellular infiltrates and exudates as well as glial and other hyperplasias. Assuredly there is nothing whatever specific in respect of these pathological "lesions," for they are a banal feature of the action of such totally different etiological factors as those of syphilis, tubercle, rabies, trypanosomiasis, poliomyelitis, and what not. Under the microscope it is impossible to distinguish rabies from epidemic encephalitis; the cortex of tuberculous meningo-encephalitis—so far as mesenchymal change is concerned—bears the closest resemblance to that of general paralysis. Or take the glial knots and nodules once imagined characteristic of typhus; they are found as a fact in a whole series of diverse pathological states associated with toxic-infective conditions—the very latest being yellow fever (cf. Jakob and Fialho¹¹). And what of perivascular demyelination? It is seen in Schilder's encephalitis, in disseminated sclerosis, neuromyelitis optica, post-vaccinal encephalitis, some cases of measles encephalitis, and the vague "acute disseminated encephalomyelitis" that is once again arousing interest. Whether one or other of these is or is not accompanied by other reactions that may conceivably serve to differentiate is immaterial to my argument; I urge strongly that the data allow of only one conclusion—namely, that perivascular demyelination is itself nothing else than a tissue reaction common to a number of conditions which differ clinically *toto caelo*; it cannot be taken by itself, and of itself, to constitute a disease in any scientific sense. When my friend and colleague Dr. Godwin Greenfield,¹² in his latest contribution to this subject, declares that "acute disseminated encephalomyelitis is a disease *per se*, which may be brought on or directed against the nervous system by certain febrile or exanthematous diseases," I answer that he is erecting a mere tissue reaction into a disease, contrary to all the canons of nosology; and that his assumption that one disease can "bring on" another disease demands the most critical scrutiny. Only if proof were one day forthcoming of the causation of this particular histological reaction by one and the same virus, invariably, inevitably, and uniquely, could it possibly attain specific value.

But illustrations need not be multiplied. This general conception of the essential non-specificity of neural tissue reactions, whether mesenchymatous or parenchymatous, has so impressed me for a long period now by its substantial truth that I consider it unassailable. The newest corroboration comes from the distinguished neuropathologist of Munich, Professor Spielmeyer¹³; I quote from his Mayo Foundation Lecture of December, 1929.

"The same alterations are found in a lesion from trauma, intoxication from carbon monoxide, intoxication from morphine, chloroform narcosis, hypertension, pseudo-uraemia, and other spasmodic conditions. Always the same alterations are seen. They are different only according to their age and intensity. When in the past they sometimes seemed to be different in

localization and there seemed to be something really typical in them, further experience showed that that was an error. *So these findings mean nothing in the definition and classification of disease entities.* Their fundamental value, rather, consists in showing something common to all these diseases, *etiologically and clinically so very different*; not anatomical forms of disease, but similar pathogenic complexes. . . . It can be seen how the most varied injuries, by a more or less long chain of causes, finally lead to the same pathophysiological process." (Italics mine.)

These are weighty words; they represent with exactness the conclusions I myself reached some time ago; though applied by Spielmeyer more especially to vascular disturbances, they stand for a principle capable of much wider application. What the neuropathologist sees is a tissue response, the expression of a pathophysiological process; one and the same process is capable of being called into being by etiological factors differing among themselves and causing clinical symptoms also differing in their type.

One or two other questions of pathological interpretation remain for brief allusion.

Such expressions as "acute haemorrhagic encephalitis," "acute disseminated encephalomyelitis," "acute parenchymatous degeneration," and other analogous terms, are merely descriptive names for pathological reactions; they correspond pathologically to such clinical expressions as "headache" or "paraplegia," and are devoid of meaning from a nosological or etiological standpoint. And it is of prime importance to note that *differing* reactions may and do sometimes occur in the *same* affection. For example, parenchymatous degeneration without obvious mesodermal hyperplasia characterizes some cases of epidemic encephalitis, as is now fully recognized; further, a number of disease conditions—for example, epidemic encephalitis, rabies, neurotubercle, neurosyphilis, and still others—may exhibit both types of reaction in one and the same case, in different parts of the neuraxis, and seemingly in complete independence of each other. Attention has lately been directed by Jakob,¹⁴ Spielmeyer,¹⁵ and other workers to the occurrence in the cortex of regions of general parenchymatous necrobiosis, pale or bleached in appearance, often without well-delimited margins, and visible only in Nissl preparations. They are best seen with a low power. Whether they are of vascular origin does not concern us for the moment; what is significant is their identical development in morbid conditions that differ *fundamentally* in etiology and in clinical character, and their coexistence with, but separation from, reactions of mesenchymal type. Clearly, the inference is again justified that some of the morbid states which we have thought constituted disease entities possess no specific pathological reaction on which to base that assumption; while, on the other hand, a seemingly definite pathological reaction is common to a number of diverse clinical states.

A final consideration bears on the question of modifications undergone by nerve cells during the normal activities of life and after dissolution has set in. Histological differences between resting and actively functioning cells are sufficiently well known; an extensive series of studies by Dolley¹⁶ has demonstrated the orderly sequence whereby changes in the quantity and distribution of chromidial substance and variation in the nucleus-plasma ratio are natural results of activity and depression. After activity, indeed, a cell may be practically dechromatinized and yet recover its full complement of chromatin during rest. The details of these changes need not delay us, but their import should not be overlooked. For in the examination of nervous tissues after death departures from the pattern of the resting cell do not all of necessity indicate the existence of pathological circumstances; on the contrary, they may equally well be physiological, and equally, therefore, indicative of health and not of disease.

Analogously, it becomes of cardinal importance to note that in toxic conditions, as well as in "natural" conditions, changes take place in nerve cells in accordance with the period after infection at which tissues are fixed and examined. This has recently been well demonstrated by Barros.¹⁷ He has injected tetanus toxin into guinea-pigs and shown by the microscope that if the tissues studied are fixed two hours after inoculation the ganglion cells of the spinal cord yield a normal Nissl picture; if

after six and a half hours, the cell exhibits early chromatinolysis; if after seventeen, it presents much more definite resemblance to the ordinary picture of a toxically degenerating cellular element. Evidently a toxin may be at work dynamically interfering with cell function before histological change can be detected.

The general bearing of these various observations, to which some discussion has been allotted, will not escape the inquiring mind. They indicate the desirability, nay, the necessity, of regarding "disease processes" as calling forth vital efforts to cope with noxae; many symptoms are proof of health, many "lesions" are evidence of attempts at repair. Along such lines of thought, I believe, we shall gain a truer insight into the activities of the nervous system.

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INFLAMMATION OF THE DIAPHRAGM.*

BY

ALBERT RAMSBOTTOM, M.C., M.D. MANCH.,
F.R.C.P.,

PROFESSOR OF CLINICAL MEDICINE, UNIVERSITY OF MANCHESTER;
HONORARY PHYSICIAN, MANCHESTER ROYAL INFIRMARY;
EXAMINER IN MEDICINE, JOINT BOARD OF
ENGLAND.

(With Special Plate.)

INFLAMMATION in the neighbourhood of and implicating the diaphragm is fairly common, but the symptoms resulting vary enormously in their severity; they may be anything from a slight discomfort in the side to those suggestive of an acute abdominal condition. Some of the cases which I have chosen to call chronic may exist, I think, without any symptoms, while some of the misleading and urgent symptoms of acute pneumonia may be the result of implication of the diaphragmatic pleura in the inflammatory process. For descriptive purposes I propose to divide the subject into two parts: (1) Inflammation of the upper surface, or diaphragmatic pleurisy. (2) Inflammation of the under surface, or subdiaphragmatic abscess. It must, however, be remembered that inflammation of the upper surface may produce symptoms resembling an acute abdominal condition, and that inflammation of the under surface may, on account of the distribution of the phrenic nerve, produce pain about the shoulder in the supraclavicular region.

It would here be convenient to remind you of the innervation of the diaphragm. Excluding the sympathetic fibres, the diaphragm receives branches from (a) the phrenic nerves, (b) the lower six or seven intercostal nerves. The phrenic nerve arises from the third, fourth, and fifth cervical nerves, but mainly from the fourth. It arises from the same segment of the cord from which the supraclavicular region receives its cutaneous nerve supply, thus accounting for pain being referred to the supraclavicular region—the so-called shoulder-tip pain of diaphragmatic pleurisy. On reaching the diaphragm most of the phrenic nerve fibres pierce it and are distributed on its abdominal surface. The phrenic nerves contain afferent

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