Lecture 37

- Progressive paralysis, an aetiological group of diseases
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Lecture

Gentlemen!

We have often met Progressive paralysis in the course of these discussions, and in such different forms that you will have already reached a conclusion as to the importance of this group of illnesses. However, the main theoretical significance of the group is far greater: For, alone among all the psychoses, cases in this group show almost constant anatomical findings, and in addition, as we also know, the constancy of this finding corresponds with constancy of certain symptoms common to almost all cases; while, beyond that, very different localization of the disease process is also to be found, but with corresponding differences in symptomatology. Thus, it gives us an example of a brain disease in which anatomical findings and symptoms correspond with one another. Of course, up to now this principle has applied only to symptoms arising in the projection system, and to the symptom of disintegration, namely dementia. However, by analogy it is permissible to conclude that what applies here, applies also to an equally large diversity of clinical psychiatric pictures, if one were in a position to locate these clinical pictures symptomatologically. Thus, progressive paralysis offers us a way into a general anatomical foundation for the psychoses. You see, gentlemen, that from this point of view, we again need to hold to the view that progressive paralysis represents no more than an aetiological recapitulation of psychoses, which otherwise differ widely from one other.

Paralytic aetiology shows itself to be related most closely to toxic effects, with the sole difference that it is a toxic effect to be seen as arising repeatedly anew within the organism. The progressive deleterious character of the disease can be explained in no other way. This necessary concept can be explained by analogy with the spinal disease *Tabes dorsalis* [W] and an assumed 'metasyphilitic toxin' [Ed], in contrast to the syphilitic aetiology. Despite this, you still cannot avoid accepting bacterial action as the basis for this peculiar behaviour. But I want to comment here that sporadic exceptions to this deleterious progression are to be seen. Over the years,

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however, amongst thousands of cases of severe paralytic psychosis with a clear syphilitic basis, a few cases have recovered completely, and not relapsed. As you can see from these comments, I perceive paralysis to be the epitome of syphilis-related psychoses, a viewpoint finding increased general recognition, and which appears justified by experiences in our Clinic. It would already be clear to you from my periodic utterances that a certain psychosis cannot be said to have an *exclusive* [Ed] causal relationship to syphilis. You can never recognize anything more than the *preference* [Ed] of a particular aetiology for a particular form of illness.

With this restriction, you must consider as specific to paralytic psychosis, the fantastic grandiosity, that is the earlier-mentioned (p. 219) *expansive* [W] form of *autopsychosis* [W], seen almost exclusively in the context of syphilis. But I have already alluded (p. 220), though not often, to the occurrence of Kahlbaum's [1] so-called *Progressiva divergens* [W], which probably was not syphilitic—and I presented to you the case of an 86-year-old woman with the same fantastic grandiose delusions—which certainly was not. The fantastic grandiosity, like other yet-to-be mentioned, and more distinct psychoses, often forms the first stage of a composite psychosis [2] usually lasting only weeks or months.

The *prodromal symptoms* [W] of progressive paralysis, usually accompanied by feelings of severe illness, are well known. They consist of headaches, insomnia, and irritable mood, and can precede outbreak of acute psychosis by 1–2 years. However, quite often, headaches are denied. In this prodromal stage, often indistinguishable from severe neurasthenia, you often also hear complaints of forgetfulness and failing ability to perform, although these symptoms cannot be verified objectively. However, early on in some cases, and in this prodromal stage, symptoms derived from the projection system may be prominent. To recapitulate briefly, they usually consist just of a suggestion of facial palsy or tongue deviation; the so-called 'paralytic speech impediment' [Ed]; and a tremor of the *voice, tongue, and lips*. The *paralytic speech disorder* [W] ranges between two opposites, which we can describe as 'stumbling over syllables' [Ed], and blurring of speech—if you prefer to avoid the anatomical terms of cortical and bulbar speech disorder. To assess stumbling over syllables, you can use test words to be repeated, like 'civilization' [Ed], 'army reorganization' [Ed], 'extraterritoriality' [Ed], etc. The voice becomes tremulous, up to the point of aegophony. If these symptoms, which are decisive indicators of palsy, are missing during the prodromal stage, diagnosis may still be possible, as soon as you can detect characteristic spinal symptoms. These *spinal symptoms* [3] [W] sometimes precede all other paralytic phenomena, and are therefore the most valuable diagnostic tools. Here, they indicate no more than signs of the so-called 'column disease' [Ed] of the spinal cord, symptoms derived partly from dorsal columns, partly from lateral columns. From the former, one must expect rigidity of the pupillary reflex. Without doubt, little value can be placed pupillary inequality. I particularly draw your attention to certain characteristic signs of combined columnar disease, although there are two types that are equally valid: Respectively, they are increased passive mobility of the legs with simultaneous increase of tendon reflexes; and reduction of passive mobility, producing prominent rigidity, together with reduction or even a total absence of tendon reflexes. Through prolonged observation, we see one of these patterns being replaced by the other; for example, return of a lost knee jerk! As regards their diagnostic value, it is important to note that in neurasthenia there may be an increase in tendon reflexes, but never a reduction.

As for the immediate precipitant of the illness, undoubtedly strenuous mental activity has often preceded it. However, we would be giving a false impression if we took into account only the 'quantum' [Ed] of work; we often see men with unceasing and strenuous mental activity who reach their later years full of vigour. Indeed, I would like to suggest that strenuous mental work is even beneficial to health. What is harmful by itself is to work under emotional pressure. Whoever finds himself forced to work beyond

his individual strength, under tight time pressure, taking on responsibilities beyond his capacity, must struggle with excitement, grief, and sorrow which can easily lead to impairment in purely. Undoubtedly all-pervading careerism encourages such damage. From this fact, and similarly from the increased prevalence of syphilitic infection, we can explain the significant predominance of the male sex, particularly amongst educated classes. The age of maximum risk is between 30 and 50 years, especially 35–45.

Alongside expansive autopsychosis we find paralytic mania; in this respect I refer again to my earlier remarks (p. 219). Usually, the picture of mania is coloured by simultaneous presence of fantastic grandiosity. At other times, it is not so pure, in that hypermetamorphosis or hyperkinetic symptoms accompany the mania. Nevertheless, cases of almost pure mania of paralytic aetiology undoubtedly occur [4]; and after running its course, only very rarely is there complete recovery, although there is often very good remission over a prolonged duration. At other times, the mania subsides, but is transformed into a more restrained state of simple fantastic grandiosity.

Affective melancholia may also have a paralytic aetiology, even if it is not usually entirely pure but rather an admixture with either mild delusions of relatedness, or symptoms of anxiety psychosis, or both, these being foreign to pure melancholia. It is widely known that melancholia occurring in the age range 35–45 years raises suspicions of paralysis.

Depressive melancholia of paralytic origin has already been mentioned. Here, too, delusions of relatedness are frequent additions, so that the differential diagnosis of pseudomelancholia comes into question.

Amongst paralytic allopsychoses, I stress the importance of *paralytic delirium* [W]. In contrast to previously mentioned forms of paralytic psychosis, which occur preferentially in initial stages of the illness, the delirious condition can appear in any phase of the illness, often quite suddenly and unexpectedly. In most cases, it is therefore not difficult to make a correct diagnosis. Incidentally, the clinical picture can be the same in all detail as that of *Delirium tremens*, as already emphasized (p. 174). However, this is nevertheless rare. Mostly, one is struck by the dominance of the twilight state, and the impossibility of patients being awakened from this state. The most obvious outward feature is clouding of the sensorium, so that one can speak of a *paralytic stupor* [W]. Delirious features that add a peculiar colour are often no more than adjuncts derived from the projection system through muscle or vocal tremor, and muscle rigidity. Instead of restless movement, akinetic behaviour prevails.

Of other allopsychoses, I must mention one case in which the purest picture of presbyophrenia showed up in its delirious form for several days. Its nature was then clarified as a case of paralysis, when a paralytic attack occurred, with subsequent specific paralytic symptoms derived from the projection systems. Instructive as the case is for relations between concepts, I introduce it only as a rare occurrence. Of the hallucinatory allopsychoses, I remember an equally rare case involving a prostitute, who was in the clinic for 2 years as ‘chronic hallucinosis’ [Ed] to be presented as such every semester. You will remember that, at her last presentation, to my surprise, symptoms derived from the projection system became noticeable, which shed light for us on the paralytic aetiology, a diagnosis which was confirmed during the subsequent course. Moreover, with regard to acute hallucinosis there are cases with paralytic aetiology whose true significance becomes apparent only after the paranoid stage has ended, through striking deficits, loss of retentiveness in memory, and paralytic speech disorders. However, exclusion of alcoholic pseudoparalysis (see later) is often difficult, and can be achieved only through a detailed knowledge of the case history. Here, I want to mention that the belief about the rarity of hallucinations in paralysis, which is still widely held, is quite wrong. In our clinic, we have had many acute paralytic psychoses in which hallucinations were represented as strongly or even more so, than in corresponding cases of different aetiology.

When discussing anxiety psychoses, I have already stressed (p. 149), that they often have a paralytic aetiology. In particular, hypochondriacal anxiety psychosis raises suspicions of

paralysis, as indeed does the large class of somatopsychoses which provides some of the most severe cases of paralysis. I already mentioned examples, amongst which bouts of most severe somatopsychic disarray and disorientation occurred, one of which led later to a purely demented form of paralysis (p. 163). However I must also include here an earlier-mentioned case (p. 74) of severe hypochondria that I cited as an example of residual hallucinosis, with a favourable outcome after acute psychosis. Already, in this first illness there was a suspicion of paralysis, since a history of syphilis was known. After 5 years of perfect health, a relapse occurred, this time taking the form of expansive autopsychosis whose deleterious course led to death within a year. A case with the most rapid course deserves mention here. Initially there was a simple intestinal somatopsychosis for some weeks gaining no fantastic significance, and it was treated as a genuine intestinal disorder. However, this was followed by a phase of hypochondriacal symptoms, which were quite fantastic in character: The patient described schemes that were running through his brain, in which an entire factory operation, with all manner of manipulations was going on; and soon it developed into the most severe threatening hypochondriacal delusion. Amongst other things, the patient had been tormented over the last few weeks by a tiger lying on him and tearing away at his liver. The entire course of illness in this 38-year-old man lasted 4 months. It had been preceded 10 years earlier by syphilis and had been treated several times. When total sensory psychosis occurred, as already mentioned (p. 273), acute worsening psychoses occurred, presenting in paralytic form, as a so-called 'galloping' [Ed] form of paralysis. Moreover, in such cases, at the very beginning or in the subsequent course, symptoms of threatening hypochondriacal delusions become clear. During cases mentioned, Affective states that are downright fearful made themselves manifest, but sometimes, according to the severity, with content of different coloration; and in other cases, which fortunately are more frequent, just the opposite is seen. The most severe hypochondriacal presentations show themselves with hardly any Affective component, such as having no head, no heart, no lungs, no stomach, or being completely hollow, 'only a tube' [W], as one educated patient put it so starkly. This phenomenon stands on its own, in no way dependent on the dementia, which may show up at about the same time. You will find a typical case of this sort in the patient presentations from my Clinic [5]. However, for weeks, in an earlier acute stage of his illness, the same patient presented the picture of most severe somatopsychic disarray, admittedly not as agitation, but only as almost total inaccessibility and helplessness, while only occasionally were there isolated expressions and actions pointing to total loss of bodily orientation.

With regard to motility psychoses of the paralytic variety, I have already often mentioned the hyperkinetic variety. Usually their manic features, fantastic grandiosity, and hypermetamorphosis are mixed together, this clinical picture developing mainly at a later stage of the illness, over several weeks. If worsening sensory psychosis reaches maximum severity, then hyperkinetic symptoms often join in with the paralytic aetiology [6]. A relatively frequent event, I should emphasize here, is the isolated *loquacity* [W] of *paralyzed patients* [W], a loquacity linked to flight of ideas, yet without any specific hyperkinetic shading, and also without actual mania. This peculiar isolated loquacity in otherwise apparently circumspect behaviour is limited almost completely to paralytics, the only exceptions known to me being the mildest cases of circular mental illness. Isolated hyperkinetic-parakinetic symptoms such as verbigeration, and stereotyped movements are met with very often in paralytics at later stages. You will remember that I have often used paralytics to demonstrate just such symptoms. Even in their relationship with aphasia and paralysis, these cases are sometimes very instructive. A type of *Echolalia* [W] may be touched on briefly here. It is occasionally seen in paralytic patients at the same time as severe motor disarray, producing such a rapid 'reflex' [Ed] reaction that it is uttered simultaneously, rather than being repeated later. You will find an example of this in patient presentations [7] from my

Clinic. Incidentally, elsewhere one usually finds responses in echolalia limited to a one- to two-syllable echo, sometimes in patients who are already quite demented, and in expressionless paralytics. The following conversation would be relatively typical:

'Are you big?'
'Big.'
'Are you small?'
'Small.'
'Are you a husband?'
'Husband.'
'Are you a wife?'
'Wife.' etc.

Akinetic motility psychosis in progressive paralysis is encountered relatively rarely in pure form, given that widespread muscle rigidity of paralysis originates specifically in the spinal cord. Hints of it are not so rare in later stages. However, in some cases that I know, prominent akinetic motility psychosis appeared as the first acute stage of the paralysis, followed by a second stage of agitated sensory confusion, and then a third stage of paralytic dementia with paralytic seizures. Every so often, you meet clinical pictures exhibiting a peculiar mixture of a paralytic delirium with akinetic motility psychosis. Moreover, akinetic-parakinetic conditions that obtain special coloration through predominance of motor disorientation and disarray should be mentioned [8].

Finally, I do not want to omit mention of certain twilight conditions, with clouding of the sensorium, which occur after paralytic attacks just as they do after epileptic attacks; usually they have certain focal symptoms, for example, combined with signs of sensory aphasia, and they tend to regress after lasting several days.

If we survey the whole picture of progressive paralysis, in so far as it can be regarded as a genuine psychosis, then in most cases, it is virtually the very model of a composite psychosis, passing successively through all different stages. Each stage may be a pure, simple psychosis; yet usually the clinical picture includes strange components, amongst which common falsifications of memory should not be forgotten. One of the more frequent possible combinations is one in which a stage of fantastic grandiosity is followed by one of mania, with allopsychic disorientation, and finally a stage of marked hypochondriac symptoms. However, just as often, a course is observed which is widely regarded as specific: cases of simple psychosis, distinguished from other simple psychoses only because of their rapid transition to dementia, and an admixture of above-mentioned symptoms derived from the projection system. Alternatively, it amounts to a colourful mixture of ever-changing symptoms, and thus to a complex clinical picture related only remotely to each simple psychosis.

The regular outcome in dementia here supports the view—highlighted at this time particularly by C. Westphal [9]—that paralysis almost always allows one to detect early signs of dementia. This is true even for cases developing just as simple psychoses, in which, by the nature of their entire clinical picture, more detailed analysis is often impossible in this regard. Nonetheless, the easiest symptom to establish here is reduced attentiveness, albeit not absolutely attributable to dementia. Even this loses its significance when there is a very severe Affective reaction. On the other hand, there are cases where no trace of deficit or loss of attentiveness can be found, like the examples of paralytic mania already cited. Fantastic grandiosity in such cases does presuppose a definite deficit in judgment, since the reality of things is apparently ignored; however, herein we find a contradiction that is no greater than the known fact (and in my opinion also wrongly evaluated as a symptom of deficit)—the failure that all mentally ill people show, to criticize the veracity of their hallucinations. Incidentally, you can find an example of paralytic mania *without* [Ed] fantastic grandiosity in my *Krankenvorstellungen* [10].

In a substantial proportion of cases, progressive paralysis follows a course, not as one or several periods of psychosis, but as a more regular progressive dementia—sometimes more regular, sometimes more intermittent—a continuous form that has led to it being designated *Dementia paralytica* [W]. I come back to this course when

I deal with acquired dementia. In all such cases, either prominent spinal symptoms or paralytic attacks with subsequent focal symptoms, can be found, occurring at the same time. Loss of mental acquisitions comes about here without the circuitous route of some other psychoses, just as does the gradual increase of direct focal symptoms in organic mental illness; it begins with autopsychic deficit, and ends in physical disorientation.

Included in the latter course, the most uniform and continuous trajectory is manifest as a curve, rising slowly in its extent, and actually belonging amongst the chronic psychoses. Whenever actual psychoses appear during the course, the illness always shows an acute character, at least temporarily, and Meynert [11] explicitly classed it with the acute psychoses.

Gentlemen! This description is still not enough to capture the multifaceted picture of progressive paralysis. It lacks some of the variations in intensity of the disease process that become established in most cases of longer duration and, may represent stages in the more-or-less uniform progression of the illness. These variations show up in opposite ways as remaining aspects of the illness: as the so-called remissions, and as acute exacerbations—the so-called paralytic attacks. *Remissions* [W] are often immediate outcomes of acute paralytic psychoses, most often with paralytic grandiosity, or specific paralytic autopsychosis as already mentioned, or of paralytic mania. One can usually differentiate remissions as being good or bad, by indications of insight into symptoms of illness in acute psychosis. If insight into the illness does not appear, while just the acute symptoms of illness disappear or abate, remission usually lasts only for weeks or months. However, in exceptional cases, even this incomplete remission (in an anatomical sense), as judged by the criterion of insight can lead to definitive recovery. This was so in a case known to me for 13 years, in which lack of insight in the early years was shown through repeated complaints, sometimes quite extreme, about our clinic. Good remissions are characterized not only by insight into the illness but also sometimes by almost complete disappearance of deficit symptoms. Quite often such a remission progresses to provisional cure, that is, one lasting more than a year and a day.

The *paralytic attacks* [W], as Lissauer [12] (see later: p. 290) first noted so incisively, undoubtedly signify an increase in acute features of a disease process, already known to be present. I come back later to discussing the anatomical findings, but note here that current monographs deal with progressive paralysis in a wholly inadequate way on this one point, relapsing in a questionable way into antiquated ways of thinking. I restrict myself to the most essential clinical data: Paralytic attacks are sometimes simple fainting episodes, or even just attacks of vertigo, while at other times they may be longer-lasting states of syncope, sometimes apoplectiform, sometimes epileptiform seizures. At the beginning of the illness, simple fainting or attacks of vertigo are to be seen, almost always followed by a short-lived speech impairment and faciolingual paresis. After a duration of hours or days, such symptoms tend to dissipate. The speech disorder can differ greatly in severity, but can amount to motor aphasia for a short time. Apoplectiform seizures can be very similar to apoplectic attacks of organic brain diseases; they usually leave behind hemiplegia or hemiplegic symptoms in a wider sense, such as hemianopia, sensory or motor aphasia, unilateral paralysis of the trunk, tactile anaesthesia of one hand, etc., generally matching the usual picture of fresh hemiplegia. Epileptiform attacks are sometimes *actual* [Ed] epileptic seizures, resembling exactly those of epileptic neurosis; however, they show a remarkable propensity for recurrence, and meet criteria for *Status epilepticus* [W]. More often the pattern of the attack corresponds more closely, or entirely, to that of the so-called cortical epilepsy, in that initially, without loss of consciousness, a specific muscle area such as the faciolingual region is affected, the onslaught then spreading further with the familiar regularity. In addition, these bouts of cortical epilepsy tend to leave focal symptoms in their wake, including, quite remarkably, even those of a sensory nature, such as sensory aphasia or hemianopia, and often also combined sensory symptoms right up to the level of asymbolia. Such focal symptoms tend to

disappear rapidly, often within a few hours; but once seizures of this type have appeared, they tend to recur in just the same form. Accompanying focal symptoms then tend to last longer and longer, and finally to remain as permanent features. It is from such cases that Lissauer [12] derived his fundamental views on paralytic seizures. That bouts with bulbar and spinal character can occur in progressive paralysis was first shown by Cl. Neisser [13] in a commendable work. Severe paralytic seizures are also associated with a significant rise of body temperature.

If we start by disregarding focal symptoms arising in the wake of the paralytic seizures, then each case is clinically important as a portent of detectable emergence of dementia. Following a paralytic attack, but especially after each series of such attacks, there is a stage of stupor, whose regression follows slowly, step by step to a degree of dementia more severe than seen before. With regard to the frequency of paralytic seizures, there is hardly a single case where they are not at least hinted at. About half of all attacks are quite prominent, while a lasting residue of distinct focal symptoms is seen in only a fraction of cases. After bed-rest as treatment was generally introduced, paralytic attacks in our clinic became relatively rare. One encounters exceptional cases where apoplectiform or epileptiform seizures with subsequent focal symptoms dominate the clinical picture, so much that they must be attributed to organic brain diseases, according to clinical criteria. Such *atypical cases* [W] of paralysis have likewise been studied in greater detail by Lissauer [14], and their anatomical findings established.

In the *course* [W] of paralytic psychoses, the clinical form taken by each illness has some influence, as I repeatedly indicated. Moreover, the duration of individual cases, right up to the lethal outcome, differs widely and can range from a few weeks—galloping forms—to more than 10 years. On average, a large proportion become patients for a period of about 1¼ years from the time of entry into institutional treatment.

Gentlemen! *Diagnosis* [W] of progressive paralysis is easy in most cases, since the combination of a distinct psychosis with the above-mentioned symptoms deriving from the projection system is quite characteristic, especially if the latter show up in near-complete form, and at the same time, dementia is already prominent. If cortical or spinal symptoms are rare, the following points should be considered: Chance occurrence should always be considered when a spinal disease coincides just with a psychosis, for example, when a person with *Tabes* [W] or spastic spinal paralysis or a chronic myelitic focus suffers acute psychosis with no internal connection between the two illnesses. In such a chance concurrence (which, in my experience, is extremely rare), the case history will then indicate that an independent spinal cord disease existed long before. More frequently, actual paralytic psychosis is combined with pronounced paralysis arising in the spinal cord, and simple paralytic dementia is most likely to develop. These cases have been well distinguished as a *worsening form* [W] of paralysis, or have been assigned the name *Taboparalysis* [W]. Meynert ascribed to them a particularly rapid course, evidently having in mind only cases of actual paralytic psychoses, not those of simple paralytic dementia. If there is no historical evidence of long pre-existing spinal cord disease, then, detection of the so-called dorsal column or lateral column symptoms, or more definitely, a combination of both with the near-universal symptom of reflex rigidity of the pupil in paralytic disease of the spinal columns, the diagnosis of a paralytic psychosis can be made safely. A mere difference in pupil size, shown by the existing light reaction has long been known to have no diagnostic value. It should be noted that certain symptoms of *Tabes*, such as gait disturbance, or the Romberg sign can be completely concealed by the increased sense of personal agency in paralytic mania. Similarly, it should be considered that psychosis could coincide with cortical symptoms just by chance. In this respect, it is particularly important to recognize that each earlier phase of motor aphasia, though outlasted successfully, and otherwise well-compensated, can leave behind prominent, long-term, stumbling over syllables. It has already been emphasized repeatedly that certain paralytic psychoses meet diagnostic criteria through their specific clinical form.

The main difficulty in diagnosis is not psychoses of other aetiology, but organic brain diseases. An especially difficult case here is that mentioned earlier, of atypical paralysis designated by Lissauer as 'abnormally localized' [W]. Such cases are definitely not to be diagnosed as deriving from foci of organic brain disease, especially when you consider their great rarity, compared to the relatively common occurrence of cortical epilepsy in tumours of the cortical mantle. Apart from such cases, the main task is differential diagnosis from cerebral syphilis, and probably as much from gumma, as from syphilitic endarteritis, or from the frequent combination of both. The main criterion here is maintained insight into the illness, which is found for cerebral syphilis. If there is even *any* [Ed] underestimation of existing focal symptoms, one is led to suspect paralysis. The speech disorder is not such a useful criterion, for the reason given above; rather more useful is the very characteristic disorder of handwriting, arising from a combination of irregular tremor and paragraphia. If focal symptoms have developed slowly with no previous apoplectiform or epileptiform seizures, this favours neurosyphilis rather than paralysis. By its very nature, the clinical picture of paralysis can develop later out of that of cerebral syphilis; and corresponding to this, transitions between the two illnesses occur quite often. You will find an instructive example of this in my patient presentations [10]. You will readily grasp that this question is of utmost importance, since in paralysis we have an illness that is no longer influenced by specific treatment, whereas cerebral syphilis requires most energetic anti-syphilitic treatment, but is then curable.

Diagnosis of a paralytic attack claims an independent significance. Gentlemen! You are so often called to deal with a so-called 'stroke' [Ed] that your first question must be whether you are dealing with a possible paralytic attack. If you find that the attack is not simple apoplexy but also includes increase in temperature and epileptiform symptoms, then paralysis becomes more probable. As always, a careful case history is the only way to find out whether familiar prodromes of paralysis had preceded the attack, or whether a dizzy spell with transient speech disorder had occurred earlier, or that signs of mental disorder had been noted. If you learn of any earlier-striking dementia dating from a particular point in time, and if you are dealing with the most common age of paralysis between 35 and 45 years, then the probability is very high. Usually the behaviour of the pupils can be used diagnostically, because pupillary rigidity is one of the most common spinal symptoms of paralysis [3]. Other spinal symptoms are unlikely to be useful, since the apoplectic attack can lead either to a flaccidity or—admittedly more rarely—to some degree of limb rigidity. However, it should be noted that the very hemiplegia of a paralytic attack can be identified because, very early on—that is after 1–2 days—it may be associated with reduced passive mobility. The timing depends on return of spontaneous movement, which is always to be expected very soon after the paralytic attack. Moreover, the hemiplegia of a paralytic attack has no special features; at most it could be emphasized that in a paralytic attack conjugate deviation of the eyes, and sometimes of the head as well, to the opposite side is more common than in attacks of the so-called organic brain diseases. The hemiplegia of the paralytic attack is usually quite short in duration, sometimes only a few hours, but more often a few days. It usually tends to regress completely, as does existing motor aphasia or other focal symptoms. Therefore, you can understand the great importance of having a proper diagnosis, to predict the near future. Of course prognosis for the distant future in a paralytic attack is much more gloomy. On the other hand, if you are faced with an apoplectic or an epileptic attack, or *Status epilepticus* [W], then the differential diagnosis is to be made in comparison with genuine or symptomatic epilepsy or the so-called eclampsia where, in any case, the medical history—and where necessary a urine test—will provide evidence. Blood sampling is absolutely contraindicated in a paralytic seizure.

Gentlemen! In terms of *treatment* [W] of paralysis, certain tasks fall to the medical practitioner. I confine myself just to general measures, mainly in the field of prophylaxis. If you know that your patient has previously survived syphilis, and you find the prodromal symptoms I have

described, or other symptoms of the so-called cerebral neurasthenia, or if there is perhaps a marked predisposition to disorders of the nervous system, or to psychosis, you must not shy away from the most drastic measures to counter the impending danger. However, anti-syphilitic treatment is indicated only when existing syphilis can be detected, be it in the brain, or in other organs; and then it is to be carried out with the utmost caution, so that any weakening of the constitution, especially a decrease in body mass, is avoided. The first condition for initiation of such treatment must therefore be that the patient curtails his occupation, and soon finds himself in the role of patient. Any measures applied while the patient pursues his occupation are often quite unhelpful. The most expedient is any invasive treatment combined with long-term bed-rest and over-feeding. If there are no traces of florid syphilis, antisyphilitic treatment is contraindicated. However, potassium iodide administered in small doses (from ½ to 1 g per day) over a long period, appears to work favourably. Nevertheless, the main thing is to enhance nutrition and correct those noxious influences that we have come to recognize as immediate causes of paralytic psychoses. Should occupational activities bring such damaging effects with them, the patient should not shy away from interrupting them for a half to a full year and, when this is ineffective, should not flinch from giving them up altogether. An investigation of spinal or cortical symptoms of paralysis will usually provide the criteria you need, to decide about such interventions.

If you no longer have any doubt, and paralysis is established to be present, it is your job to bring it to an end as quickly as possible, since any delay results all too frequently in material and social ruin of the whole family. If you are in any doubt over whether and when to bring the patient into a mental institution, it is always safest to decide in favour of this. Admittedly, in many cases, a specialist will postpone the date of containment for a long time.

Anatomical findings [W] in progressive paralysis are best described by dividing them into macroscopic and microscopic. The *macroscopic findings are* [W] prominent only after the illness has run a prolonged course, since it represents mainly the end result of a florid anatomical process, just as cirrhosis forms the outcome of liver disease. The outcome is atrophy of the cerebral cortex, most obviously in its documented loss of weight. This loss is not spread evenly across all parts of the cortical mantle, but, averaging across brains, the greatest shortfall occurs in the frontal lobe—although it should be noted that the frontal lobe in Meynert's [11] sense also included the anterior central gyrus. However, this average conceals the fact that isolated cases preferentially involve temporal, parietal, or occipital lobes; or, for these three lobes, or when there is mainly a bilateral illness with the same localization, 'abnormal localization' [W] does occur, as the atypical cases of Lissauer prove. I have assembled the following values from Meynert's table, which has never been surpassed by more recent authors in the care taken in weighing, and in the number of cases. In a substantial proportion of cases, weight loss also involves the brain stem. The cerebellum seems always to be least affected, so that from it, one has figures for comparison with values for other regions.

Taking brain-weight of manics to be approximately normal, their averages (in grams) were:

	Total weight	Cerebral cortex	Brainstem	Cerebellum
39 males	1,376	1,082	148	146
53 females	1,221	957	131	133

Paralytics, on the other hand, gave averages of:

	Total weight	Cerebral cortex	Brainstem	Cerebellum
145 males	1,215	933	135	146
29 females	1,068	819	119	130

The parts of the cerebral cortex had the following proportions amongst manics:

	Total weight	Frontal lobe	Temporal lobe	Occipital lobe
Among men	1,376	450	251	380
Among women	1,221	404	213	339

Amongst paralytics, on the other hand the proportions were:

	Total weight	Frontal lobe	Temporal lobe	Occipital lobe
Among men	1,215	380	216	337
Among women	1,068	323	202	294

Apart from loss of weight, atrophy is expressed by visible change on the brain surface and in the ventricles. On the brain surface there is more or less extensive loss of cortical substance, distributed in a very irregular way. Often the entire cerebral cortex, and at other times large sections of it, show reduction in the cortical grey substance of up to half or a third of the normal width; occasionally you even find scattered locations where cortical substance is missing entirely. The medullary strips of the gyri and the common underlying white matter are likewise revealed as significantly narrowed. Corresponding with this atrophy of the cerebral cortical substance, there is usually an increase in free cranial fluid, as *Hydrocephalus externus* [W].

The reaction of the pia mater shows two contrasts. Most obvious by far, you find that the pia is relatively soft, although often cloudy, the latter again especially over the frontal lobes, and thus the pia adheres so firmly to the brain surface that it appears to have fused with it. In any case, if you try to separate the pia, shreds of brain tissue remain adhering to it, often to a great extent, but often also only on the crests of the gyri [Ed], and there remains an ulcerated cortical surface, which soon turns reddish on exposure to the air. This so-called *decortication* [W] was formerly taken to be evidence of widespread inflammation of the brain surface—'periencephalitis' [W] or 'meningoencephalitis' [W]. People have usually distanced themselves from this view, since microscopic examination does not confirm the interpretation. From experiences in our clinic, this is almost always a sign of maceration, which takes a little time to form. If one has the opportunity to perform an autopsy soon—or only a few hours—after death, it is almost always possible, with caution, to avoid the decortication. Only a small proportion of cases prove to be exceptional, where examination of thin slices reveals real adhesion of the pia to the brain surface. It is known that the same phenomenon of decortication occurs in other conditions favourable for maceration, especially when cortical tissue is pressed against the tightly stretched translucent pia by *Hydrocephalus internus* [W], in meningitis or by a brain tumour, and the convolutions are flattened outwards and against one another. In contrast to these main cases of decortication, one often also encounters the opposite reaction, of a markedly thickened pia, richly saturated with fluid and usually also hard to tear. In these cases the pia tends to be very easily removed from the brain surface without any loss of substance.

The gyri differ in their prominence, with many depressions and pleats, corresponding to the grade of atrophy; their texture is apparently thickened. In all old cases, you also find expansion of ventricles and *Hydrocephalus internus* [W], a sign of general atrophy. Ventricular walls are very often abnormally firm, presenting the so-called *Ependymitis granulosus* [W] found especially at certain preferred sites, and this can even extend to the fourth ventricle. I hasten to add that despite this finding on the ventricular surface, hydrocephalus is no more than a result of diffuse atrophy, arising to fill the vacuum. We also find such consequences in the roof of the skull and in the dura mater. In the roof of the skull diffuse thickening is often present with no other structural deviation. Sometimes, however, there is a more-or-less widespread loss of diploë, and a type of eburnation. This finding might be interpreted independently as syphilitic bone disease. Frequently changes of the so-called *Pachymeningitis haemorrhagica* [W] are to be found on the dura mater, usually by chance, and undiagnosable in life. These consist in part of isolated blood stains, and their organized remnants, and in part as recent signs of major bleeding next to multiple membranous formations left as residues from previous haemorrhagic episodes. Only rarely does the extent of the bleeding reach as far as the base of the skull; usually it is mainly the convexity that is affected and one hemisphere

can also appear flattened by such a pool of blood. However, it is most likely that atrophy of brain substance and the vacuum so created first precipitates these bleeds. As regards symptoms of haemorrhagic pachymeningitis, I have already noted that, in my own view, even cases in late stages of paralysis with very prominent anatomical changes are usually undiagnosable. Only in the case of unilateral papilloedema, which has often been observed when the bleed extends right into the sheath of an optic nerve (according to Fürstner [15]), will diagnosis sometimes be possible.

In some cases, especially in the atypical form of paralysis mentioned above, a gross anatomical finding of marked atrophy of the optic thalamus on one or on both sides can be seen in addition to the above findings. The white *Stratum zonale* [W] of the thalamus may thus appear grey over large stretches, the appearance being altered so much that for example the pulvinar protrudes like a sharpened ledge; and the texture becomes spongy. Lissauer's work grew from such findings.

All the above changes can easily be regarded as *sequelae* of the underlying process of tissue destruction as revealed in *microscopic findings* [W], whereas earlier, following Virchow's [16] doctrine of inflammation, the belief was always that there was a primary process of inflammation in the supporting vascular tissues, and in the neuroglia. For true insight into the real process we should thank Exner [17], for his discovery of the abundance of myelin in the cerebral cortex, and Tuczek [18], for his work based on this. Perfection of Weigert's [19] method of staining myelin sheaths, and the work of Lissauer have provided us with the most significant advances in our knowledge. (Preparatory work for a comprehensive publication is included in part in the posthumous draft of a habilitation thesis. A revision of this manuscript, often understandable only to the most well-informed, is one of the next tasks for the workers in my clinic. It will emerge from this, just how far Lissauer was ahead of all his co-workers in his penetrating knowledge of the paralytic process. His only publications on this are given below: [12, 14])

In what follows, I restrict myself just to the quintessential, and most important microscopic findings, stressing that I have secure knowledge of modern neuroscience teaching and how it is applied to disorders of peripheral nerves and spinal sections in degenerative neuritis. Primary disintegration and necrosis of neural elements, analogous to degenerative neuritis in the peripheral nervous system, is, from the onset, and throughout the course, the essential process determining all symptoms of paralysis. Earlier changes in supporting vascular tissues and in fibres of glia-like cells, which have been taken as signs of primary inflammation, are secondary or reactive to changes resulting from the primary necrosis of neural structures. They are thus consequences and outcomes of the illness, a *quasi-scar* [W] formation, replacing healthy tissue, not the actual disease. The disease is generally progressive and pernicious, so that I had earlier [20] drawn a parallel between it and progressive muscular atrophy. We can explain this by the presence of a constantly-unfolding toxic effect which has the specific effect of causing degeneration of the neural elements of the central nervous system, mostly in the cerebral cortex. Necrotic decay is detectable first in axons, but they are to be regarded as the main targets of toxicity only because they are dependent on nerve cell bodies for their nutrition. Corresponding to this, the first success was to detect degeneration of nerve fibres; and indeed we have known since Tuczek that axons are usually lost initially in the most superficial cortical lamina that which Meynert [21] identified as the first, purely grey lamina. Later, the network of fine fibres in supraradial and intraradial layers is affected, and finally the radii themselves. At first, cell bodies seem to be quite unchanged. However, in later stages, one concludes [20] that there is significant cell loss in all layers of the cortex, so that the cell layers become uniformly narrowed. In addition, I have always found cortical sites where the number of ganglion cells is visibly reduced, and the microscopic appearance of the cortex is changed in such a way that, instead of the normal, regular, and delicate delineation, a disorganized jumble of fibres, cells, and glial components is found.

Now it is known from the work of Nissl and his successors [22], that ganglion cells of the cortex, in every case of paralysis, also suffer severe changes. (Nissl's methylene blue stain is equivalent in its importance for pathology of the ganglion cells as is Weigert's myelin sheath stain. The reader will find information about the method in refs. [23] and [19]; see also [23, 24].) However, credit for first finding cell shrinkage of the entirety of the cortical layers undoubtedly goes to Lissauer. This researcher succeeded in proving, in cases of atypical 'abnormally localized' [W] paralysis, a laminar degeneration in those cortical regions in the parietal and occipital lobes which were identified as the point of onset of the focal symptoms. Cell loss in these cases did not extend continuously over the cortex, but came in irregularly-distributed patches, and involved mainly layers of densely arranged, small pyramids, arranged in rows, and increasing in size inwards, in other words, Meynert's second and third layers. Macroscopically this can be identified on the hardened brain as a bright stripe running parallel with the cortex, in the middle of the grey cortical substance, darkly stained by chromium solution. These cases also enabled Lissauer to show that secondary degeneration of myelinated fibres from these locations could be traced through the otherwise intact medullary white matter to other locations, and especially downwards into the corona radiata and internal capsule; and that generally changes of the white matter in paralysis are consistently based on secondary degeneration. Clinically, Lissauer's atypical cases were distinguished, in that mainly only focal symptoms of the parietal and occipital lobe were present, namely loss of tactile sensation and hemianopia, and that these had developed in connection with paralytic attacks in the manner indicated above. 'The paralytic attacks then appear as a sudden violent surge of the paralytic process in certain cortical territories.' That the changes in the white matter were largely to be regarded as systematic, was already highlighted by Tuczek, who emphasized especially that the degeneration he demonstrated in six cases, in the shortest association bundle lying just deep to the cortex—Meynert's *Fibrae propriae* [W]—always involved sites where myelin degeneration of the cortex was also prominent.

In Lissauer's cases, thalamic tissue also showed itself to be abnormal, providing evidence that secondary degeneration occurs in subcortical ganglia whose importance von Monakow has rightly emphasised. Moreover, this degeneration leads to disappearance of axons and cells, so that only coarse spongy tissue remains, within which the regular, delicate markings of thalamic tissue are completely missing. According to the type of focal symptom, different regions of the thalamus showed themselves to be changed in this manner, confirming Monakow's [25] theory of the thalamic nuclei. The anterior region of the thalamus and the lateral geniculate body appeared to be unaffected by secondary degeneration in cases mentioned, while the medial geniculate body behaved as the other nuclei of the thalamus, with secondary degeneration and sensory aphasia as a result of the paralytic disease of the temporal lobe.

Lissauer's findings show that the paralytic process can differ greatly in intensity and extent, so that, at certain locations, it can progress to actual paralytic focal disease in the cortex and that this progression becomes manifest in the form of paralytic seizures. The white matter pathology consistently shows the hallmarks of secondary degeneration. (This sentence from Lissauer finds striking confirmation in the work of Starlinger [26]). Thus some fundamental empirical facts have been gained, that are no less important than Tuczek's work.

Regarding the localization of the paralytic process, the following should be noted. In all his cases, Tuczek found the frontal lobe to be involved, and had come to the view that fibre loss generally progressed in an antero-posterior direction, and would go no further than the region of the central gyri. However, in contrast, Zacher [27] had already found that the parietal, occipital, and temporal lobes were also abnormal, sometimes more so than the frontal lobes, and that Tuczek's statement that fibre loss always started in tangential fibres of the outermost cortical layer, only later to involve the deeper layers, had no general validity. Lissauer's findings also

suggest that the paralytic process has a very irregular, patchy distribution, by no means beginning exclusively in the outermost cortical layer. Common to virtually all cases, however, is a remarkable fibre loss in the insula, Broca's gyrus [28], and the lower extent of the central gyrus, corresponding to clinically detected speech disorder, and paresis of the faciolingual area in almost all cases. Such mainly focal localization, as in the other atypical cases, is however very rare.

Moreover, it is noted that the paralytic process is not limited to the cerebral cortex: Beyond the thalamus, other subcortical regions can also be affected. Thus, A. Meyer [29] demonstrated loss of myelinated fibres in the cerebellar cortex; and H. Schütz [30] showed that the myelin of the periaqueductal grey matter and motor cranial nerve nuclei had been attacked. Perhaps the diversity of paralytic seizures is connected with this.

Since Weigert has taught us about normal distribution of glial cells in the brain, we are also in a position to evaluate also the localization of glial cell proliferation. Amongst other things, Meyer's finding in the cerebellum is confirmed in Weigert's [31] great work. Proliferations of glia arise everywhere where neural parenchyma have degenerated; therefore, the location of this indicates localized loss of nerve cells. At a particular stage in such proliferation, we have observed the occurrence *en masse*, of giant astrocytes; and indeed they correspond to the more recent stage, seen temporarily soon after loss of neuronal tissue. Later, for the most part, they disappear again, but a proliferation of fibrous glia remains permanently. In some cases, however, such a glial reaction fails to occur; and all that remains are regions with a wide-meshed net of normal glial fibres forming rarefied stripes or patches.

Recently Binswanger in his careful monograph [32] obtained similar results with regard to the primary parenchymatous nature of the disease. We learn from him about occurrence of inflammatory changes and, where it applies, disintegration of adhesions of the pia to the cerebral cortex. 'Destruction of cortical tissue, with its consequences, leads to greater accumulation of pathologically-altered lymph fluid in the extravascular lymphatic system. It drains mainly into areas formed by glial sheaths and areas for collection on the brain surface. Here the accumulated lymph fluid of dying tissue changes by coagulation and hyaline necrosis, but it also evokes hyperplastic processes in the adjacent pia and its vessels. In consequence of the latter, partial adhesions of the brain surface to the pia mater occur, with scleropathy of large sections of the epicerebral space, relocation of the confluences of extra- and intravascular lymph spaces.' It is readily apparent that in this way the outermost cortical layers can easily succumb to a maceration process after death. Moreover, it seems to me that Binswanger overestimated the influence of these processes on the course of the disease, and he is particularly mistaken in their application to paralytic seizures.

Gentlemen! If you ask me what final result is to be drawn from these cortical findings for the theory of illness, it is briefly as follows: The paralytic process almost always leads to rapid loss of neural elements of the cerebral cortex, which is significant, but subject to great local variation in its extent. According to Meynert [11] loss of weight within a year amounted to about 100 g. Corresponding to this is the dementia that accompanies the course of the illness in most cases from the outset. This dementia is therefore dependent on the extent, not the localization of the paralytic process, and is thus to be regarded clinically in its entirety. Preferred localities for early attacks, as described above, correspond on the other hand to the most frequent cortical symptoms derived from the projection system. With this concept there need be no surprise that Zacher also found extensive loss of fibres in the cerebral cortex among senile, alcoholic, and epileptic demented patients, and that this has been confirmed many times since. Here too, breakdown of the clinical phenomena coincides with anatomical findings.

As for the changes in the spinal cord, they are certainly based in part on secondary degeneration, for example when, in late stage of the illness, general helplessness occurs, with muscle rigidity and increase in tendon reflexes. On the other hand, the above information on premature recurrence of spinal symptoms in paralysis

reveals that severe illness of the spinal cord often takes place independently. The connection with the paralytic process in the brain is evidently the production of the same active toxin. We also know from the *Tabes dorsalis* [W] that it, like paralysis, is a *sequela* of syphilis. That at one time only the spinal cord is affected, while at other times, the brain is involved exclusively or predominantly in a form of paralysis, and that *Tabes* [W] sometimes persists as such, while at other times after existing for many years, can still lead to paralysis, must be considered as depending on the respective predisposition of different individuals and particularly on the functional harmfulness of the process.

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