ON CERTAIN PROBLEMS PRESENTED BY CASES OF GENERAL PARALYSIS WITH FOCAL SYMPTOMS.*

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General paralysis presents many problems both to the clinician and to the pathologist. The clinician meets these problems at every stage of the disorder, and a merely casual review of their nature would already bring us into contact with almost every other important group of mental disorders. Even where the diagnosis is clear, the meaning of the various elements in the clinical picture, and the reason of the great variety in the relative prominence of the individual symptoms are quite obscure. The differential diagnosis of general paralysis in its incipient stages from certain functional psychoses, from conditions due to exhaustion or to the action of various poisons, is not always easy; in the later stages it may be extremely difficult to differentiate between general paralysis and other organic dementias arising on the basis of cerebral syphilis, brain tumor, cerebral arteriosclerosis, senile brain atrophy, etc. In the clinical picture of the organic dementias focal symptoms frequently play an important rôle, and in this communication I propose to discuss some points with regard to the focal symptoms in general paralysis.

Focal symptoms may be present in a case of general paralysis without there being any evidence of a direct relationship between the cause of the focal symptoms and the general paralysis; this is, for example, what is found in certain cases with traumatic lesions. I may refer to a case of general paralysis with complete anosmia, recently observed in the clinical service of the Psychiatric Institute. The anosmia was due to the destruction of the

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olfactory lobes by a fall in the hunting field, which occurred thirty years before the onset of the general paralysis.

In cases with traumatic incidents the situation is not always so clear as in the patient with anosmia of traumatic origin. One of my patients had on two occasions a rather severe injury in the period of the insidious onset of general paralysis; on the second occasion there was evidence of fracture of the base of the skull, followed by a traumatic delirium. In the clinical picture which the patient presented under observation, aphasic symptoms and weakness of the right side were present in addition to the physical symptoms of general paralysis. At the autopsy there was found some cortical softening in the peri-sylvian region, but even after microscopical study of this area it was difficult to say what rôle had been played by the trauma and by the general paralysis respectively in its causation.

I have mentioned these cases merely to indicate the general range of the topic, and shall pass now to cases where the focal symptoms are more intimately related to the general paralysis. They may be related only indirectly to the general paralysis, inasmuch as they have their origin in the same syphilitic infection; they may be related very directly to the general paralysis and be due to the special severity of the paralytic process in definite regions of the cortex (Lissauer's atypical paralysis).

I shall begin with a case of a very familiar type. The patient, a janitor, at the age of 33 had a left-sided hemiplegic attack without loss of consciousness; the attack left slight permanent weakness of the left side. Nine years later the insidious onset of general paralysis began, the disorder ran a typical course and the patient died at the age of 45. The post-mortem examination disclosed the typical histopathological changes of general paralysis; in addition there was endarteritis obliterans, with aneurysmal dilatation and occlusion of the cerebral vessels which had caused a sub-cortical softening in the region of R. F. 3.

A hemiplegic attack at the age of 33, in the absence of valvular heart disease or any general infection may in the majority of instances safely be attributed to a syphilitic disorder and usually arises on the basis of an endarteritis obliterans (Heubner's type). In the present case the autopsy confirmed this view. We had to deal therefore with a case of general paralysis which, at an earlier

period, presented evidence of syphilitic cerebral vascular disease. In view of the fact that general paralysis seems only to occur in patients who, at a long antecedent date, have had syphilis, it is not at all to be wondered at that at an earlier period the brain, its vessels or its membranes, should be affected by the syphilitic poison. In such a case the neurological history of the patient is divided into two periods separated by a long interval of time; the incidents of the early period seem to have little to do with the history of the later period, and the evolution of the general paralysis seems in no way influenced by the residuals from the earlier period. At each stage the diagnosis was clear to the clinician; the pathologist could easily demonstrate two processes side by side—the special type of degeneration of the larger vessels, and the characteristic histopathological changes of general paralysis.

The situation is not always so clear as in the above case, and the history of the following patient shows an evolution in which the different stages are by no means so clearly delimited.

The patient, a journalist, had a chancre in 1898, for which he was treated during a period of 6 months; in 1901 he had diplopia, which improved under potassium iodide. In April, 1902, he had an attack of weakness of the left side, which came on during a period of 24 hours, without loss of consciousness; the diagnosis of cerebral syphilis was made. The patient improved under treatment with potassium iodide. In November, 1902, he had a second attack of left-sided weakness, with transitory inability to speak, but without loss of consciousness. He received hypodermic injections of mercury, and also took sodium iodide; under this treatment he improved. During the following three years he suffered from occasional headache, and in 1905 he was unable to keep his position. He complained of increasing weakness in the left leg, he fell on more than one occasion; he complained that his memory was failing. From January to August, 1906, he was in a hospital where he had vigorous anti-syphilitic treatment; he received as much as 390 grains of potassium iodide daily, he was also treated with hypodermic injections of mercuric salts. During this period he had convulsions on several occasions; he was sometimes restless and noisy, he wanted to take a stroll along the river, he had hallucinations of hearing, and was apt to ramble on about imaginary things.

In August, on admission to the clinical service of the Psychiatric Institute, he was childishly happy, affable, loquacious, amused by details. He admitted that he had no grounds for his euphoria, and said that he had "not a damn'd cent"; as to his physical condition he said "it's a terrible plight—I don't suppose I will ever get well again"; he laughed cheerfully at the situation. The patient complained of his memory being poor, but was able to give a connected account of his life; he made several careless mistakes, but was able to correct these as a rule. He said that the interval between the two admissions to the N. Y. Hospital on the occasion of his hemiplegic attacks was 18 months, when as a matter of fact it was only six. He was very much confused over the incidents of the immediate past, confused his present environment with the hospital from which he had come.

Physical status: left-sided hemiplegia, not involving the face; no sensory disorder; the left knee-jerk was more exaggerated than the right; tremor of hands and face; the pupils, equal but irregular, reacted well to light and on accommodation; the speech was tremulous and sticking, but without any distortion of the words even in difficult test phrases; the writing was extremely tremulous, the words were crowded up into one corner of the paper, but were correctly written. Ten days after admission the patient had a series of convulsions, with special involvement of the right side, leaving some weakness of the right arm and marked paraphasia; he died 12 days later.

The cortex showed the characteristic histopathological changes of general paralysis; there were several foci of softening, one involving part of R. F. 1, of R. F. 2, and of the upper fourth of R. A. C, another involving the head of the left caudate nucleus and the anterior fourth of the putamen on the left side; foci of softening were also found in the marrow of the left occipital lobe and in the pons. There was well-marked endarteritis obliterans.

In this case the clinical history does not divide itself into such distinct periods as in the previous case, but seems to present the evolution of one process in which no definite line of demarcation can be drawn. There is not, as in the previous case, the long incubation period intervening between the first series of neurological incidents and the later onset of a process of a different kind. In the present case the clinical picture of brain syphilis passes insidiously

and without any long incubation period into that of general paralysis. The whole course of the disorder, its early incidence after the initial infection, the nature of the early symptoms, viz., diplopia, headache, hemiplegic attacks, and in the later period the absence of grandiose ideas with the retention of fair insight into his physical decline and into his defective memory seemed to indicate brain syphilis; the euphoria was a somewhat striking feature, but we know that it frequently is found in cases of brain syphilis; the memory defect, in its setting of a certain mild confusion and difficulty of orientation, could not be considered pathognomonic of general paralysis. At the beginning, therefore, the process appears to have been that of brain syphilis as evidenced by the close relation to the initial infection, by the symptomatology, by the pathological evidence of endarteritis obliterans with consequent focal softenings, while at the end there was no doubt about the process of general paralysis, as evidenced by the typical histopathological changes in the cortex.

At what stage in the evolution of the patient's sickness did it take on the serious character associated with the progressive changes of general paralysis? After all we must remember that we have no grounds for maintaining the unitary nature of the changes in general paralysis. Thanks to the researches of Nissl and Alzheimer we have a definite histopathological criterion which enables us to group our cases uniformly according as they do or do not satisfy that criterion. That this criterion is not the essence of the process is evident from the fact that Nissl found the same histopathological changes in the cortex of a dog and two rabbits. The importance of the histopathological criterion is that it enables us to start from a homogeneous group when we discuss the subject of general paralysis, and that it makes possible a common understanding. The meaning of these histopathological changes is quite obscure, and Nissl himself has raised the question whether they represent a unitary process or whether certain elements in the pathological picture may not be a direct syphilitic manifestation, while other elements may represent a process of a different type.

In the clinical history of the foregoing case we face a series of incidents and a development which become more intelligible if conceived as the expression of more than one process, one pro-

cess not merely succeeding the other, but having its own evolution side by side with the other.

The difficulty of coming to a decision as to whether a case is one of general paralysis or of brain syphilis is further exemplified in the following case; the clinical history was in many respects similar to that of the previous case, no final clinical diagnosis could be made, the autopsy disclosed multiple gummata in the brain.

The patient, a janitor, 47 years of age on admission, contracted syphilis in 1891, at the age of 33; in the summer of 1900 he had strabismus of several months duration. In September of the same year he had an attack of dysarthria and staggering; in September, 1901, weakness of the right leg developed, his speech was somewhat defective. From this time on he had residual weakness of the right leg and during the following two years he had several attacks or right-sided weakness with involvement of speech; on one occasion he was said to have had an attack of weakness of the left arm. In July, 1905, he had an apoplectiform attack followed by a stuporous condition and delirium of several weeks duration, which led to his admission to the hospital in August. In October he developed transitory left-sided ptosis. At that date his physical status was as follows—weakness of the right face, arm and leg; on both sides sign of Babinski and ankle-clonus; left internal ophthalmoplegia; the right pupil reacted slightly to light, well on accommodation; fundi normal; the speech was slurring, slightly sticking, without omissions or transpositions, but with the occasional insertion of *r*; the writing was tremulous with omissions and distortions, *e. g.*, “methis espical” for methodist episcopal, “bittililery” for artillery; lymphocytosis of the cerebro-spinal fluid. Particular attention was paid to an analysis of the mental state of the patient as the diagnosis was a matter of considerable doubt. On admission he was a trifle excited and pugnacious, but soon settled down to a condition of placid good humour; he said that he was happy, felt first-rate; he did not resent being with crazy people; he knew the date, called the place “Manhattan Life Insurance—Bellevue Hospital.” He gave a rather poor outline of his life with marked discrepancies in his dates. He had no adequate realization of his general condition. During his hospital residence his mood continued

to be one of exaggerated complacency with a tendency to whimper when talking of home. He felt that he could resume his old work, but showed no megalomaniac trend. This mild euphoric dementia, with the type of memory defect presented by the patient, pointed in the direction of general paralysis, and the nature of the writing defect seemed to support this diagnosis; the neurological history with its varied incidents seemed to point more in the direction of cerebral syphilis. We have, however, already seen from the preceding case that such a neurological history is not incompatible with the development of general paralysis. The unilateral ptosis with complete fixity of the left pupil was the most definite evidence of cerebral syphilis; in the preceding case, however, diplopia had been one of the earliest symptoms.

The autopsy showed general cloudiness of the pia, frontal atrophy, ventricular granulations; there was a gumma in the left centrum ovale, another in the right parieto-occipital fissure; an old softening of vascular origin was found in the right internal capsule and thalamus, another in the left side of the hind-brain involving the pyramidal tracts; the larger vessels showed a definite endarteritis obliterans. The cortex showed preservation of the general structural arrangement; there was no diffuse plasma-cell infiltrate. The meninges showed a syphilitic meningitis of varying grade with slight extension into the cortex; this is a form of syphilitic disorder to which Dr. Dunlap has especially called attention, and which approaches most closely the condition found in general paralysis.

If I have reported these two cases in somewhat tedious detail, it is because I feel that the difficulty of differentiating clinically between general paralysis and cerebral syphilis is not sufficiently realized; it is true that certain symptoms have considerable value in pointing very strongly in one direction or in another, but we must recognize that in a certain number of cases, even after the most careful weighing up of the various symptoms, the only honest course is to withhold a diagnosis until the microscopical examination enables us to definitely classify the case.

These considerations are still valid notwithstanding the introduction of new methods into psychiatric procedure. It has been hoped that an infallible laboratory method might enable us to

dispense with tedious clinical arguments. The introduction of the Wassermann method marks an important advance in our knowledge of general paralysis; it gives us direct evidence of the connection of general paralysis with syphilis, a connection which previously had merely the support of statistical evidence. It does not, however, always solve our clinical problems, and simply furnishes one more datum to be taken into consideration in weighing up the evidence with regard to the diagnosis. That it is difficult, even with the help of the Wassermann reaction, to determine the exact stage of the evolution of the disease in the individual case may be seen in the following case:

Gennaro P., a wood-carver, had syphilis at the age of 19; at the age of 40, in December 1907, he had an apoplectiform attack with residual left-sided weakness. After this attack he was inefficient at work, treated his wife outrageously, and finally was certified as insane. On admission he presented slight weakness of the left side, Argyll Robertson pupils, no defect of speech nor of writing, no tremor of the fingers; the cerebro-spinal fluid showed lymphocytosis and increased globulin; both the blood-serum and the cerebro-spinal fluid gave a positive result with the Noguchi modification of the Wassermann reaction (Dr. Henderson). The mental state of the patient was one of mild complacency with slightly inadequate realization of the gravity of the situation; his memory was slightly defective.

In such a case we are entitled to attribute the hemiplegic syndrome to a syphilitic endarteritis, although certain reservations on this head must be made later. Argyll Robertson pupils are not frequently found in cerebral syphilis and point much more strongly towards general paralysis. As to the Wassermann reaction it is just in such a case that we realize its limitations, for although the positive reactions increase the probability of the case being one of general paralysis, the possibility of cerebral syphilis is not excluded. The necessity of basing conclusions with regard to the differential value of the Wassermann reaction on material that is controlled by autopsy, is obvious in the light of cases such as those which have been briefly referred to.

The discussion of the above cases has shown how closely the question of the focal symptoms in general paralysis is bound up with the problem of the fundamental nature of the disorder and of its relation to syphilis.

In a paper on arteriosclerosis in relation to mental disease

read before this association at a meeting in Washington (May 8, 1907), I made a brief reference to a patient, the diagnosis of whose case was a matter of great difficulty. The patient had begun to fail at the age of 45; from that date his memory became progressively worse; at the age of 58 he had a general convulsion. During the following two years he showed progressive mental decline and a variety of neurological incidents. In view of the absence of knee-jerks, the presence of the sign of Romberg, a well-marked lymphocytosis of the cerebro-spinal fluid, the diagnosis of tabes dorsalis was made. In view of a permanent right-sided hemiplegia and right-sided sign of Babinski, with numerous transitory left-side attacks the additional diagnosis of advanced arteriosclerosis of the basal vessels with focal softening in the left occipital region was made.

The mentality of the patient throughout his stay in the hospital was that of "the lean and slipper'd pantaloons"; he was amiable and mildly jocose, but at no time showed definite euphoria and never uttered any ideas of grandeur. The writing of the patient showed very marked tremor and great distortion of the words. The reaction of the pupils to light became more and more sluggish during his stay in the hospital; the speech was extremely slurring, but did present the features which are so characteristic of general paralysis. The possibility of general paralysis was considered, but it was felt that there was not sufficient evidence to make a positive diagnosis of general paralysis. The autopsy seemed to confirm the clinical diagnosis; the vessels of the base of the brain showed a very extreme degree of diffuse thickening and the left visual cortex was destroyed by a large area of softening due to the occlusion of a thickened artery; the pia was not markedly thickened and the brain showed a rather diffuse mild degree of atrophy. In addition to the damage due to defective nutrition resulting from vascular thickening, symptoms had been caused directly by the pressure of thickened tortuous vessels; the right optic tract was reduced practically to a ribbon by the pressure of the adjacent posterior cerebral artery.

On microscopical examination the typical histopathological changes of general paralysis were found. The necessity of microscopical examination before making any final statement as to the nature of such a case is here well shown, for the autopsy gave no

indications of general paralysis. The anatomical evidence enabled one to see that in this case, as in the other cases already referred to, for a considerable time there had been going on side by side the evolution of two processes, the process of general paralysis on the one hand and on the other hand various changes due to disease of the larger vessels.

In a certain number of cases of general paralysis with focal symptoms the latter are due to the special severity of the paralytic process itself in definite regions of the cortex; such cases were described by Lissauer under the heading atypical paralysis, in contrast with the classical type of general paralysis, where the greatest severity of the process is in the prefrontal and frontal region and where focal symptoms of motor or sensory nature are absent. The paralytic process in such cases is most marked in the posterior half of the cortex, the degree of destruction is more pronounced than in the classical form, secondary degenerations can be demonstrated in relation to the affected areas; the clinical course of these cases shows certain characteristics, it is apt to be a less uniform decline than in the classical form, and to consist rather in a descent by steps, the downward steps usually corresponding to a series of attacks; the total course is apt to be longer than in the classical type, and the clinical picture frequently presents considerable difficulty in diagnosis. Between the atypical general paralysis of Lissauer and the classical type all transition forms can be found.

To the pathologist and the clinician these cases furnish extremely important problems, but in this communication I shall merely have time to take up one or two points. A case which has just recently come to autopsy is worth reporting in this connection. The long duration of the case, the stationary nature of the symptoms, the keenness of the patient and the absence of any memory defect made the diagnosis of the case extremely difficult.

The patient was a man of 37, who had followed a variety of occupations, from jockey to machinist, and been temperate in the use of alcohol; at the age of 26 he had a chancre, for which he received treatment during one month. Four years later he began to suffer from pains in the back and chest, accompanied by nausea and vomiting; during the next six years he continued to have these pains.

At the age of 34 he had a transitory episode of weakness and numbness of the left side; two years later he was diagnosed "incipient locomotor ataxia." At that time he presented Argyll Robertson pupils, diminution of the knee-jerks, slightly tabetic gait, tenderness over the hypogastrium. In the following year he began to show a grandiose trend, he wished to take his physician for a carriage ride, he talked of plans for working a patent, wished to move into a better house, he asked a girl in a store to marry him and knocked her hat off when she refused. Owing to this behavior he was certified as insane.

On admission he was talkative and elated, said that he was worth \$90,000, the patent was worth over 3 millions, he was a first-class prize-fighter; the physical status, as then noted, was, Argyll Robertson pupils, knee-jerks decreased, speech defective.

For some months the patient remained megalomaniac and somewhat excited, he then became depressed and hypochondriacal; on several occasions he had attacks of vomiting and of severe pain in the side. He had a variety of other attacks; in May, 1903, he had an apoplectiform attack which left him with slight left-sided weakness.

In the following year, in April, he had several convulsive attacks, and it is probable that the hemianopia, which was later observed, dated from this series of attacks.

In the summer of the same year (1904) he had an excited period with well-marked megalomania; he was a millionaire, owned the hospital and the White House, had been 9 million years on earth; "I am McKinley, I'm greater than God Almighty, I own the world and have got billions upon billions of dollars."

This megalomaniac condition lasted for several months and then simmered down; during the following year (1905) he showed definite depression with a marked hypochondriacal trend; his detention was unjust, his lungs and heart had been knocked out of him, his food was doctored so that his bowels did not move, nothing ever passed out of him. At the same time the patient showed excellent grasp of all relations not touching his own condition.

During 1906 there was little change in the patient's general condition, he had occasional convulsions and periods of weakness, he said that his bowels were stopped up by poison in the food,

there was steam in the bed, the mattress was charged with electricity. He did not elaborate his depressing delusions into any system; at times he was unable to resist shouting out these accusations, but at other times he would spontaneously criticize himself for this abuse, and admit the possibility that he was mistaken; perhaps the bed was not magnetized, perhaps it was merely his nerves, he might be slightly crazy; "the devil must have got into me yesterday saying such crazy things—I was calling people murderers, I must stop that, it's nonsense."

He would pay a daily visit to the physician in his office and ramble on about his experiences in life; although he would frequently refer to his unjust detention and to his morbid ideas he did not press the physician for his discharge; he would pass abruptly from bitter complaint to good-humored gossip about life in hospital and at home, he commented with much shrewdness on his fellow-patients and discussed newspaper topics in an intelligent manner. He was pleasant and humorous in his conversation, and took considerable pleasure in recounting his exploits in the past. His memory was extraordinarily good; he remembered all his transfers during his hospital residence and could give correctly the number of each ward in which he had been. He made light of his physical ailment and felt sure that he could easily earn a living; fresh air and city doctors would cure him, he could get a job as night watchman, could make money as an entertainer, could publish a book of his experiences.

The physical status in July, 1906, was as follows; residuals of a left-sided hemiplegia, slight weakness of the left face, arm, leg, sign of Babinski on the left side, impairment of sensibility on the left side, left-sided hemianopia, athetoid movements of left hand, marked ataxia of left arm and leg. The knee-jerks, diminished in 1901, were now definitely exaggerated, the right being occasionally more active than the left (due to spastic condition of the left leg). Argyll Robertson pupils; nystagmus in lateral vision, general diminution of pain sense; sign of Romberg; speech somewhat slurring, without tremor, sticking or distortion of words; writing, tremulous with marked distortion of the test words, *e. g.*, "mthosit episocpil" (methodist episcopal); marked lymphocytosis of the cerebro-spinal fluid.

During the following five years until the time of his death the

patient showed remarkably little change either in his mental or in his physical condition. He had occasional periods of depression, but as a rule was bright, alert, interested in the newspaper and in hospital affairs; a very careful examination of his memory, in 1910, showed that, apart from one or two trifling lapses, his memory was still excellent. He still talked with confidence of his own abilities, and claimed to have personal influence with the Governor; his hypochondriacal complaints were unchanged and he had a number of poorly elaborated delusions. In his physical condition there was little change, the writing was rather better than in previous years, although he distorted one letter and wrote "thirid" for third. The cerebro-spinal fluid showed a marked lymphocytosis with positive globulin reactions, but negative Wassermann (Noguchi's modification); the Wassermann (Noguchi) reaction with the blood-serum was positive (Dr. Henderson).

The patient during the latter years had a series of attacks of a somewhat peculiar nature; immediately after the attack he would be quite clear and remember every detail up to the onset of the attack. He made light of these attacks, and frequently had occasion to say, "I'm no parietic."

On May 28, 1911, the patient, at 7 a. m., had one of these apoplectiform attacks and fell heavily on his head, causing a subdural hæmorrhage; when examined at 9 a. m. he made light of the attack, protested against being detained in the hospital, stated accurately to a day how long he had been detained. Ten minutes later he became unconscious, during the rest of the day there was marked twitching of the right side of the body; the patient died at midnight without regaining consciousness.

The difficulties presented by such a clinical history are obvious. The prodromal period with apparently tabetic symptoms, the gradual onset of an elated and megalomaniac condition, the periods of florid megalomania, the pronounced hypochondriacal trend, seemed to indicate general paralysis, a diagnosis which was further strengthened by the presence of Argyll Robertson pupils and the special defect in writing. The hemiplegic syndrome—left-sided weakness, impairment of sensibility, hemianopia, with athetoid movements of the left hand, suggested in addition the presence of a focal softening involving the posterior limb of the capsule, the

optic radiations and the optic thalamus; the athetoid movements of the left hand indicated the involvement of the optic thalamus.

It was somewhat difficult, however, to reconcile the diagnosis of general paralysis with the striking preservation of the memory of the patient, and with the lack of progression of the symptoms.

At the autopsy a large recent sub-dural hæmorrhage was found over the right hemisphere; this, however, only partly accounted for the contrast between the flattened right hemisphere and the well-rounded convolutions on the left side. The right hemisphere showed a very considerable degree of atrophy in comparison with the left hemisphere, the convolutions were narrower, and although the sulci were not specially wide, this may have been due to the recent hæmorrhage. The pia did not show any definite thickening; there was no special atrophy of the frontal lobes; no granulations in the 4th ventricle were seen by the naked eye. The basal vessels were in good condition except for a patch of thickening in the right internal carotid just at its bifurcation.

On a horizontal section which passed just at the upper limit of the optic thalamus on the left side and slightly above it on the right side, the right hemisphere presented a very marked diffuse atrophy of the medullary substance, with no focal lesion; the cortex did not present any very marked difference on the two sides.

Another section was made just below the level of the middle of the thalamus on the right side without any focal lesion being found. The pons showed hæmorrhagic infarction. Numerous blocks were taken from the cortex for microscopical study and the brain was placed in Müller's fluid to be later cut in serial sections.

The microscopical sections showed the typical histopathological changes of general paralysis, which were more marked on the right side than on the left; the pia showed an exudate of plasma-cells and lymphocytes; the general structure of the cortex was disorganized, with considerable loss of nerve cells; there was a diffuse peri-vascular plasma-cell infiltrate throughout the cortex.

I do not intend to discuss the numerous problems which arise in regard to this case. I wish to emphasize one point which it demonstrates, viz., that in a case of general paralysis, of ten years' duration, with the process much less marked in the left than in the right hemisphere, the memory may remain practically intact and the general mentality of the patient may show very little evidence of progressive reduction.

The case again warns us to be careful in the use of clinical material which is not controlled by autopsy, and illustrates the value of the modern histopathological criterion. It makes us accept with reserve cases published before the last decade, for the classification of this case, even with the help of the microscopical findings, would have been extremely difficult before the publication of the work of Nissl and Alzheimer.

The fact that we correlate the left-sided syndrome with the right-sided cerebral atrophy does not mean that we have any adequate understanding of the disorder; the correlation is of a rather crude kind, and we are far from understanding the intimate mechanism of the clinical symptoms. We are equally far from understanding the factors which lead to the definite topographical distribution of the severity of the paralytic process. It is certain, however, that it cannot be explained on the basis of lesions of certain cerebral vessels, for the distribution does not as a rule correspond with vascular territories, and the microscopical examination of the vessels frequently fails to show any alteration sufficient to account for the particular severity of the cortical disorder.

The fact that a pronounced right-sided cerebral atrophy may be accompanied by such a moderate degree of mental reduction is of considerable interest, and in this context I should like to briefly mention another case, presenting several features in common with that of the patient already reported.

The patient, 47 years old at the time of his death, a tabetic general paralytic, had been over 3 years in the hospital, he had been definitely insane for 4 years before his death, he had shown slight mental symptoms for at least 9 years before his death. He had numerous left-sided attacks, with a permanent left-sided syndrome—hemiplegia, hemianæsthesia, hemianopia.

No focal softenings were found in the brain post-mortem, but the convolutions of the right hemisphere were extremely shrivelled, and furnished a striking contrast with those of the left hemisphere. The patient, however, at the time of his death was very far from presenting the extreme degree of mental reduction which is found in many patients, whose brains show nothing like the degree of atrophy shown by the right hemisphere of this patient. The description of one of his attacks, two years before death, may be of interest in this connection. On August 12, 1907, the left arm and leg began to twitch, without involvement of the face. There was

no impairment of consciousness; he was talkative, referred spontaneously to the twitching, said that he was certainly going to die in the evening. He wanted to go home and settle up his household affairs. "I know I am dying, I want to speak with my three children, to be good to the mother when I am no more. I am very sorry if I must die, I will be 45 on Christmas (correct), do for me what a poor man, a dying man, expects, put me in two blue blankets and in the ambulance, want to die with my woman." The twitching in this attack lasted for two days.

The lucidity of the patient during such an attack, with symptoms due to some active process in the right cerebral cortex, and the fact that his mental reduction later was not extreme while the right cerebral cortex showed an extreme degree of shrivelling, leads us to ask how far the degree of dementia has to be correlated more strictly with changes in the left cerebral hemisphere and not so much with the cerebral atrophy as a whole.

From this point of view it will be of interest to pay particular attention in our cases to the relative involvement of the two sides of the brain and to see whether this may help us a little further in our work of clinico-anatomical correlation.

In concluding I should like to call attention to one group of cases of general paralysis with focal symptoms, the consideration of which should prevent too premature an interpretation of the relation of clinical symptoms to the pathological findings. I refer to that group of cases where even a conscientious and systematic examination of the brain reveals no focal softenings, no focal exacerbation of the process of general paralysis, in short nothing which we can correlate with the clinical symptoms.

Out of a series of twenty cases of general paralysis with focal symptoms, in 6 there was no pathological evidence of any focal disorder; in another case with a permanent hemiplegia, which had been diagnosed previous to admission as thrombosis of the internal capsule, no lesion of the internal capsule was found, nor did the motor cortex on the suspected side show any definite difference from that on the other side. There are limits, of course, to our technical methods and an examination can never cover absolutely exhaustively the territory suspected, but the lesson from these cases is, perhaps, that we must learn to think in more functional terms of these symptoms, especially where we are dealing with focal symptoms of a transitory nature.

The points which I have desired to call attention to in this communication are as follows:

SUMMARY.

1. Cases of general paralysis may present focal symptoms which are more or less irrelevant to the general paralysis, *e. g.*, focal symptoms of traumatic origin.
2. Cases of general paralysis may present focal symptoms, which are based on a process which has a common origin with the general paralysis, *e. g.*, symptoms due to softening on the basis of a syphilitic endarteritis.
3. The evolution of a case, which at an early stage presents evidence of syphilitic vascular disease, into a case of general paralysis may be more or less rapid and the clinical picture may represent a combination of more than one process.
4. The exact stage at which the onset of the general paralysis has begun is extremely difficult to determine, even with the help of modern serological methods.
5. The clinical picture alone is sometimes insufficient to enable a positive diagnosis to be made, the autopsy itself may not be decisive, the microscopical examination of the cortex is essential for a decision.
6. The pathological criterion of certain histopathological changes is invaluable, but the relation of these changes to the disease process is quite obscure.
7. Focal symptoms in general paralysis may arise on the basis of localized severity of the paralytic process.
8. In one case reported, of ten years' duration, there was remarkably little mental reduction, but the paralytic process especially involved the right hemisphere.
9. The relation of dementia to the right and left hemispheres respectively is a problem of interest, the study of which may further clinico-anatomical correlation.
10. In many cases of focal symptoms in general paralysis the examination of the brain reveals no adequate cause for the focal symptoms; this should warn one against being satisfied with the crude correlation of the lesions, which we do find in other cases, with the clinical symptoms, seeing that the latter may sometimes be found in the absence of such lesions.