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Original Articles and Clinical Cases.

PROGRESSIVE LENTICULAR DEGENERATION: A FAMILIAL NERVOUS DISEASE ASSOCIATED WITH CIRRHOSIS OF THE LIVER.[1]

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[1] This paper formed part of a thesis for the degree of M.D. of the University of Edinburgh, July, 1911, for which a gold medal was awarded.

INTRODUCTION.

THE object of this paper is to give a full description of a rare nervous disease, of which, as far as I am aware, no instance has been recorded during the last twenty years—a disease to which, for reasons which will hereinafter become evident, the name of "Progressive Lenticular Degeneration" may be conveniently applied. The disease is familial, in the sense that frequently more than one member of a family is affected with it, but it is not hereditary; it may also occur sporadically. It occurs always in young people, either in an acute or a chronic form. As far as my present knowledge goes it is progressive and invariably fatal, its duration ranging from six months or a year to as long as four or five years. The clinical symptoms form a complex which, once the physician is familiar with it, can be readily recognized, one which is of great interest and importance, constituting as it does what may be considered to be a pure *syndrome of the corpus striatum*. In a word, it consists of involuntary movements, nearly always a bilateral tremor of both upper and lower extremities, the head and trunk also being sometimes involved—a tremor usually rhythmical but occasionally irregular, and increasing with volitional movement; there is pronounced spasticity of the limbs and of the face, the latter being usually set in a spastic smile, while in the later stages contracture of the limbs develops; there is dysphagia and dysarthria, the latter eventually degenerating into complete anarthria; there is sometimes spasmodic laughing and emotionalism. As a result of the extraordinary degree of stiffness of the musculature there is considerable difficulty in maintaining equilibrium. Little or no true paresis or paralysis occurs, however, inasmuch as most ordinary movements, if not all, can be executed, though it may be slowly and feebly. In some cases certain mental symptoms, of a transitory nature, manifest themselves, and their significance will be duly discussed. In spite of the great degree of motor weakness and helplessness, in a pure case the abdominal reflexes are preserved and a double flexor response is obtained. In other words, this affection, where it occurs in an uncomplicated form, is *an extra-*

pyramidal motor disease, the importance of which is apparent not only because of its rarity, but also by reason of the light it sheds on such diseases as paralysis agitans.

The pathology of the disease is as striking as the clinical syndrome. As a glance at the figures will show, the lesion is *a bilateral symmetrical softening in the lenticular nucleus*, involving more particularly the putamen; the globus pallidus is affected to a less extent. In addition the external capsule may be partly included in the area of disease; the caudate nucleus may be slightly degenerated, but—most important of all—in a pure case the internal capsule is absolutely intact. The optic thalamus similarly escapes. Certain important secondary degenerations follow from the lenticular disease. If the diseased areas are examined minutely it will be found that a change begins apparently round the lenticulo-striate vessels, as a result of which the substance of the lenticular nucleus begins to shrink and atrophy; its cells and its fibres disappear, and their place is taken by glial tissue, the laminæ medullares and internuncial fibres becoming less and less distinguishable; in advanced cases the nucleus breaks down entirely, and a cavity formation is the result. There is no sign of syphilitic disease of the vessels concerned, all of which are patent; their walls, indeed, often appear to be rather thinned. Gross vascular disease is conspicuous by its absence. It is clear the condition is not due to a thrombotic process in the distribution of a particular blood-vessel; on the contrary, the peculiar selective action of the morbid agent will be readily appreciated when it is remembered that the lenticular nucleus is supplied from three different sources. Yet in this disease one collection of grey matter is singled out, while neighbouring grey matter areas are left intact. Compared with this bilateral symmetrical degeneration of the lenticular nucleus and associated alterations, the other changes found in the central nervous system are slight and comparatively unimportant; they will, however, be duly recorded in their place.

What must be considered, as it seems to me, the most curious and the most remarkable feature of this familial nervous disease is the constant presence of a profound degree of *cirrhosis of the liver*. This hepatic cirrhosis does not reveal itself by any symptoms during life, nevertheless it is always found after death. It is mixed in type, as will be subsequently shown. Syphilis and alcohol, as possible morbific agents in connexion with this cirrhosis, can, I believe, be entirely excluded. This association, in young people, of cirrhosis of

the liver with bilateral symmetrical softening of the lenticular nucleus constitutes the disease from the pathological standpoint; clinically, the symptoms are exclusively nervous. Other organs (thyroid, &c.) show changes of secondary importance, to be described below.

Progressive lenticular degeneration, as the disease may be called, is not one with which the medical profession is familiar. As far as I can discover, no case has been recorded since 1890, with the very doubtful exception of one reported by Anton, of Halle, under the title of "Dementia Choreo-asthenica, with Juvenile Nodular Cirrhosis of the Liver," some three years ago. In all probability this case was one of congenital syphilis. The total number of cases of the disease that have been published amounts to six only. Of these, two (brother and sister) were reported by Gowers in 1888 under the name of "Tetanoid Chorea, associated with Cirrhosis of the Liver"; one by Ormerod in 1890; three (two brothers and a sister) by Homén, of Helsingfors, also in 1890.

Ormerod called his paper "Case of Cirrhosis of the Liver in a Boy, with Obscure and Fatal Nervous Symptoms." Homén described the condition as "A Peculiar Disease occurring in Three Members of a Family in the form of a Progressive Dementia, probably Lues hereditaria tarda." All these six cases were fatal. In Gowers's cases (both acute) no lesion of the central nervous system was found. In Ormerod's case (acute) there was slight bilateral symmetrical softening in the putamen. In Homén's cases (all chronic) the same symmetrical lenticular lesions were found in all three, together with sundry other changes to be referred to later. All six had marked cirrhosis of the liver.

Since 1890 there has been no further light thrown on the mystery of the disease, nor has there been any adequate pathological investigation, so that the subject has remained a *terra incognita*.

In this paper will be described four cases of the affection which have been personally observed and diagnosed (in all but one the diagnosis was made during life), in three of which it has been possible to make a *post-mortem* examination.

The first patient (S. T.) came under observation in 1905, and died on July 28, 1908. At the autopsy bilateral degeneration of the lenticular nucleus was found, coupled with cirrhosis of the liver.

The second patient (D. P.) came under observation in 1906, and died on March 3, 1907. Here, also, cirrhosis of the liver and a slighter degree of lenticular change were discovered.

The third patient (E. P.), a brother of the above, came under notice

in 1907. This patient was exhaustively examined in the summer of 1910. He died on September 20, 1910, and in his case identical findings were obtained at the autopsy.

The fourth patient (M. To.) came under observation in the autumn of 1911, and at the time of writing she is still living.

In addition to these four personal cases the record of two other cases of the disease has been obtained, one of which occurred in the family described by Gowers, but has not hitherto been published, as the notes were lost years ago. By a piece of good fortune I was able to trace the mother of the family, an old lady aged 70, and to obtain from her the clinical details of this new case. The other is one referred to by Ormerod in his paper of 1890; the notes, not hitherto published, are preserved in the National Hospital, Queen Square.

Thus I am in a position to add no less than six cases to the existing record, scanty as it is; and a consideration of their remarkable clinical and pathological features may help to elucidate the nature of a rare disease, which presents problems that interest the clinician, the pathologist, and the physiologist. The application of modern methods of investigation to the material at my disposal, it may be hoped, will serve to remove some misconceptions as to the nature of the affection, and to establish as a morbid entity this "progressive lenticular degeneration," on which much work yet remains to be done.

It is my pleasant duty here to acknowledge my deep indebtedness to many who have aided me in this research, which has extended over six years. My grateful thanks are due to Sir William Gowers, Sir David Ferrier, Dr. J. A. Ormerod, and Dr. H. H. Tooth for permission to utilize their notes on the cases that have been at one time or another under their care in the National Hospital, and for encouragement and suggestions in the prosecution of the work; as also to Sir Victor Horsley; Dr. James Taylor, and Dr. Holmes, of the National Hospital; Dr. W. H. B. Stoddart, of Bethlem Royal Hospital; Dr. Parkes Weber; Dr. Thomas Wilson, of Birmingham; Dr. Max Tylor, of Wisbech; Dr. W. D. Moore and Dr. G. W. Smith, of Virginia Water Sanatorium; Dr. T. R. Elliott and Dr. Otto May, of University College Hospital; Dr. F. W. Goodbody, of University College; Dr. Yunge-Bateman, of Folkestone; and Dr. Reymond, of the Sanatorium, Chexbres, Switzerland, for invaluable assistance at various times. Further, I cannot refrain from acknowledging here the extent to which my task has been lightened by the willing co-operation of different members of the families concerned, who, by their intelligent interest in a subject which cannot but have

painful memories for them, have rendered me services for which I am profoundly indebted to them.

Chapter I.—Historical.

The first two recorded cases of the disease which forms the subject of this monograph we owe to the clinical acumen of Gowers, who, in the year 1888, published in his well-known "Manual" the following paragraph, under the title "Tetanoid Chorea" (vol. ii, p. 656):—

"A case was recently under my care that presented symptoms intermediate between those of chorea and tetany. The disease was fatal, and no lesion was found after death. The patient was a boy, aged 10. A brother was said to have died from some affection similar to that from which this child was suffering.[1] There was a history of three other relations having suffered from maladies resembling chorea. In this patient the disease commenced gradually seven months before death. The symptoms consisted of tonic spasm, which was continuous, and varied by paroxysmal attacks of similar but more intense spasm. The face was involved on both sides, so as to cause a constant peculiar smile. The tongue was pressed back against the palate in such a manner as to impede swallowing and prevent speech. The arms were extended, pronated, and rotated inwards, so as to bring the back of the forearms outwards, while the fingers were generally slightly flexed at all joints, but at times were extended and slowly moved in the irregular way characteristic of athetosis. The legs were extended at all the joints, the feet being over-extended in talipes equino-varus, and the toes were flexed. At times the spasm at the hip became flexor, so that the extended legs were raised off the bed. The muscles of the trunk were also involved in the spasm. At first the left side was the more severely affected, but afterwards the spasm became equal on the two sides. The electric irritability of the muscles was normal, and there was no mechanical excitability of the nerves. There was considerable pyrexia during the more severe stage of the disease. The boy steadily emaciated, and died from exhaustion. The whole central nervous system appeared normal to the naked eye, and no distinct morbid appearances could be discovered on microscopical examination. I have not been able to find a description of any similar case."

[1] *See* footnote, p. 301.

This bare outline of an historic case, as the earliest recorded instance of a new disease must always be, leaves some points unnoticed: the fact that the boy was found to have cirrhosis of the liver is not mentioned, as its significance was not at that time appreciated. The original notes, however, preserved in the National Hospital, Queen Square, are remarkable for their fulness and accuracy of description, and in particular for the wealth of illustration incorporated with them. Copies of the drawings and old silver prints, with which the notes are enriched, will be found below.

Not long after, the sister of Case 1, a girl of 15, came under the care of Gowers, suffering from identical symptoms, which ran an identical course, and terminated fatally in a few months. Realizing the great interest of the condition, that observer republished the cases in the *Review of Neurology and Psychiatry* for 1906, in fuller detail, under the heading "Tetanoid Chorea, and its Association with Cirrhosis of the Liver." In the opening paragraph of this communication the following passage occurs:—

"These cases were under observation many years ago, and their record has been waiting for other facts that might elucidate their mystery, but waiting in vain. They are now presented in the hope they may direct further attention to these strange forms of disease."

From the original notes of these two cases the following précis has been made, in which the cardinal features of the condition, as observed by Gowers, are succinctly described from the clinical and pathological standpoints.

(The full notes of the cases will be found in the Appendix, p. 489.)

Case 1.—Sydney M., aged 10, was admitted to the National Hospital, Queen Square, London, on October 5, 1886, under the care of Sir William Gowers.

The patient was the eighth of fourteen children, and had had no illnesses except typhoid fever at the age of 3. An uncle on the father's side was said to have been affected in the same way as the patient, and to have recovered after an illness of twelve months. The eldest brother had died at the age of 15 of some form of paralysis.[1]

The symptoms began gradually, without exciting cause, three months before the patient was admitted to the hospital, with clumsiness and awkwardness of the hands; about the same time involuntary movements of the arms and legs commenced. On admission constant slowly changing movements in the limbs

[1] This is the case whose notes have been lost, but whose history has been obtained from the mother of the family, still living at the age of 70. It will be found below among the new cases (my Case 5, p. 361). There is no doubt it belongs to the series.—S. A. K. W.

attracted attention, as well as a generalized spasticity. A contraction of the zygomatics caused a continuous smile, now greater on one side, now on the other. The mouth was usually held spasmodically open, and the tongue generally back in the mouth; occasionally it was slowly protruded. When told to shut his mouth the patient used to push the lower jaw up with his hand, then the spasm of the muscles would seem to give way and he would close his mouth easily, but it returned to the widely open position in a minute

FIG. 1.—S. M. (Gowers.) The tremors, spasticity, contractures, &c., are well seen. From one of the original silver prints (dated 1886), kindly lent to me by Dr. Thomas Wilson.

or so. A great degree of dysphagia was present, and also of dysarthria; speech was usually almost unintelligible, but occasionally the patient could utter words or sentences more distinctly, especially in the morning. As he lay in bed he often made a low whining sound.

The muscles of the neck, trunk, and limbs were all involved, in varying degree, in the generalized tonic spasm; sometimes involuntary movements, not unlike athetosis, occurred in the fingers; at other times the arms and hands were definitely tremulous. The extremities were in a state of contracture, the

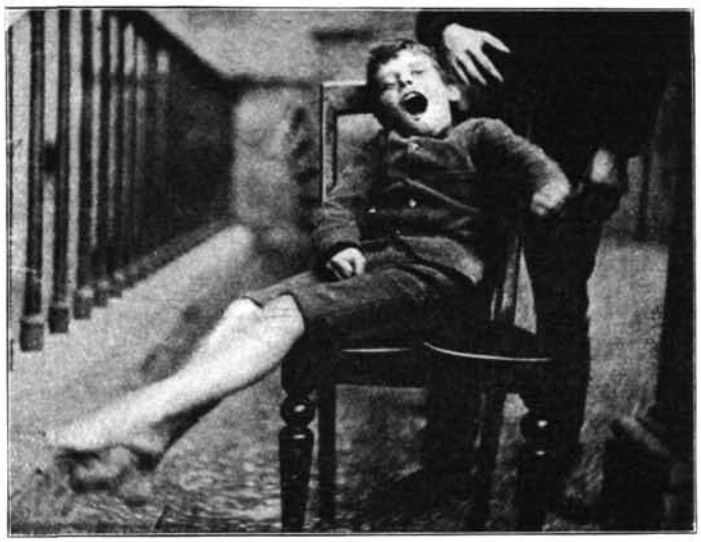

FIG. 2.—S. M. (Gowers.) Note the apparent indifference of the patient to the fact that his mouth is widely open. From the original in the notes at the National Hospital.

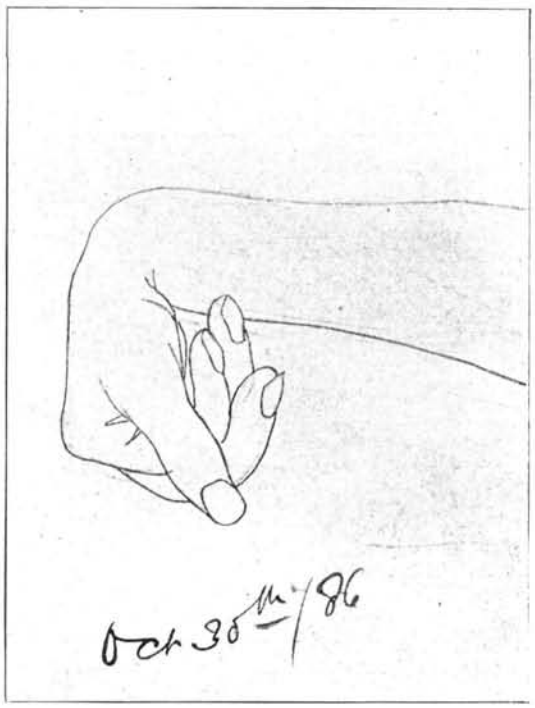

FIG. 3.—S. M. (Gowers.) From the original drawing in the notes of the case at the National Hospital.

fingers flexed, and the forearms pronated, while the feet were extended and inverted, and the toes flexed; in spite of the great degree of spasticity, occasionally it relaxed sufficiently to allow the contractures to be overcome.

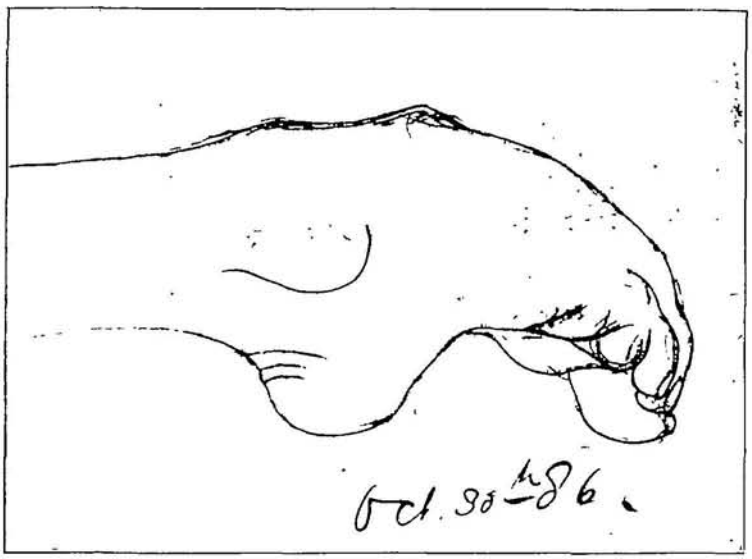

FIG. 4.—S. M. (Gowers.) From the original drawing in the notes of the case at the National Hospital.

FIG. 5.—S. M. (Gowers.) Photograph taken shortly before death, showing spastic smile, contractures, and profound emaciation. From the original silver print (dated 1886), kindly lent to me by Dr. Thomas Wilson.

Voluntary movement was interfered with by the spasm to a less extent than might be anticipated; the patient could take hold of any object with little difficulty. He was able to walk, although the heels were usually off the ground, but sometimes they came down and he walked naturally. There was

no sphincter impairment. The knee-jerks were present; ankle-clonus was not obtained. The plantar reflex was noted as "slight." (This was long before the days of insight into the significance of the plantar reflex.) The cremasteric reflex was active; the abdominal was not elicited. Sensation was everywhere

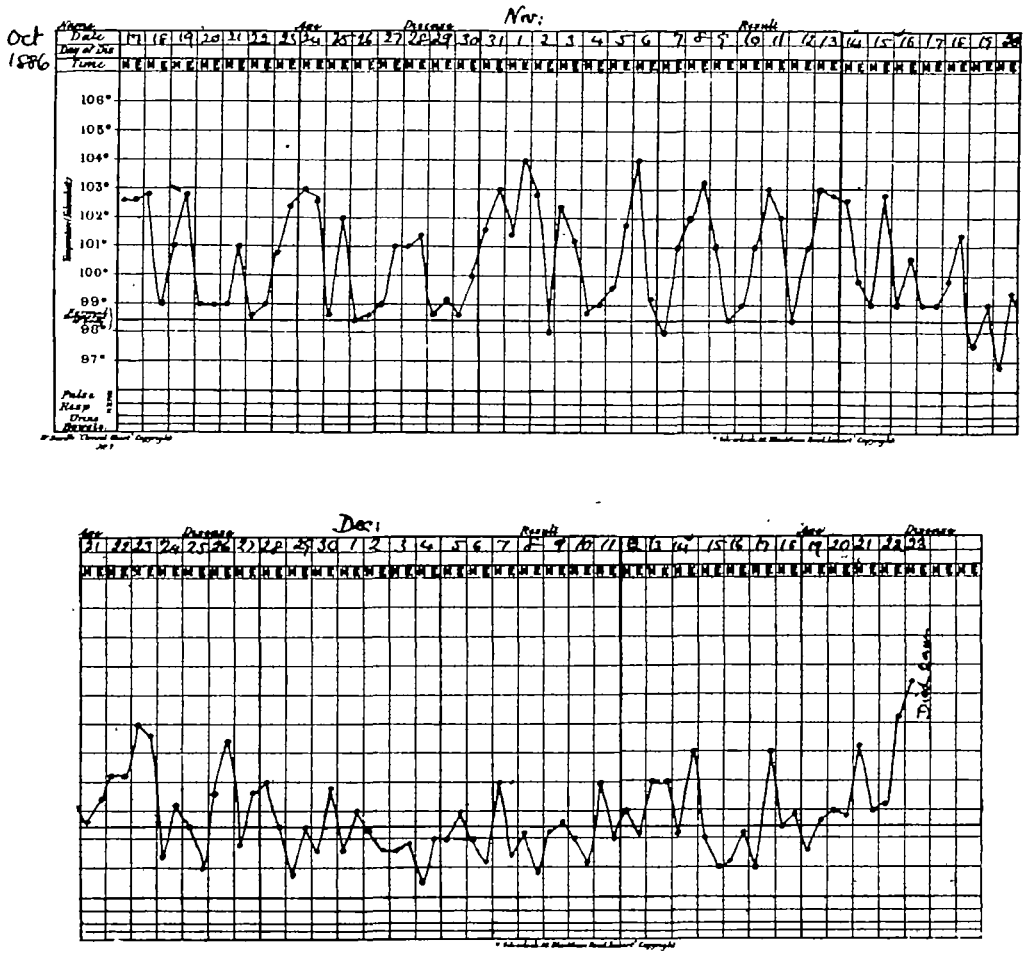

FIG. 6.—Temperature chart of S. M. (Gowers.)

normal. The optic discs were normal; the mind was clear; the patient could write down what he was unable to articulate, and evidently understood everything that was said to him.

During the first few days after admission some improvement occurred, but thereafter the patient became steadily worse. His temperature rose, and continued highly irregular (fig. 6). He became drowsy, and began to pass his urine

and stools into the bed. The dysarthria and dysphagia increased; the spasmodic contractions of the musculature became intensified; the extremities became more definitely contracted. Emaciation set in rather rapidly, and the patient gradually sank into a more and more helpless state, with the result that eleven weeks from the date of his admission, and six months from the beginning of the symptoms, he died.

A *post-mortem* examination was made. Naked-eye investigation of the brain, cord, and membranes revealed nothing abnormal. The liver was noted to be firm, hard, and lobular, and was evidently cirrhosed. Portions of the cortex, cord, peripheral nerves and muscles, examined microscopically, did not show any departure from the normal.

A glance at figs. 1 to 5, which have been reproduced partly from the photographs in the notes and partly from original silver prints, kindly lent to me by Dr. Thomas Wilson, of the General Hospital, Birmingham, who was Resident Medical Officer to the National Hospital at the time, will serve admirably to take the place of fuller description. It must be remembered they were taken before the days of instantaneous photography, hence the tremulous movements of the arms are well shown; indeed, for my purpose, this is almost to be preferred, as it accentuates the contrast between the spastic smile and wide-opened mouth and the tremors of the upper limbs. The contractures of the hands and feet are well seen. The progressive emaciation can be readily appreciated. The drawings are copied from the original sketches in the notes, depicting the condition of the distal portions of the limbs.

No one who compares these photographs of twenty-five years ago with the series illustrating my own cases can fail to be struck by the very close resemblance between them. The same spastic smile, open mouth, tremors, contractures, and emotionalism, are portrayed by the unerring camera in such a fashion as to render comment needless.

In the light of subsequent knowledge the points to emphasize in Sydney M.'s case are the following:—

A boy, aged 10, suffers from an acute and fatal illness of six months' duration, whose features suggest strongly it is of a toxic or toxi-infective nature. The only certain pathological condition found *post-mortem* is cirrhosis of the liver. Nevertheless the clinical symptoms are exclusively nervous and are from the outset severe and progressive. They consist of dysarthria and dysphagia, emotionalism, generalized rigidity of the musculature of face, trunk, and extremities, tremulous and sometimes irregular involuntary movements of the limbs, without any true paralysis, as most ordinary movements can be performed,

contractures that can at first be overcome, but gradually establish themselves permanently, and emaciation. Sensibility is intact, and there is no definite indication of direct interference with the pyramidal system.

Case 2.—Charlotte M., aged 15, the sister of Sydney M., was admitted to the National Hospital on August 29, 1888, under the care of Sir William Gowers.

She had always been a healthy girl. Menstruation began about a year before, and was quite regular for seven months, then ceased abruptly.

For the last nine months she had become listless and lethargic, and

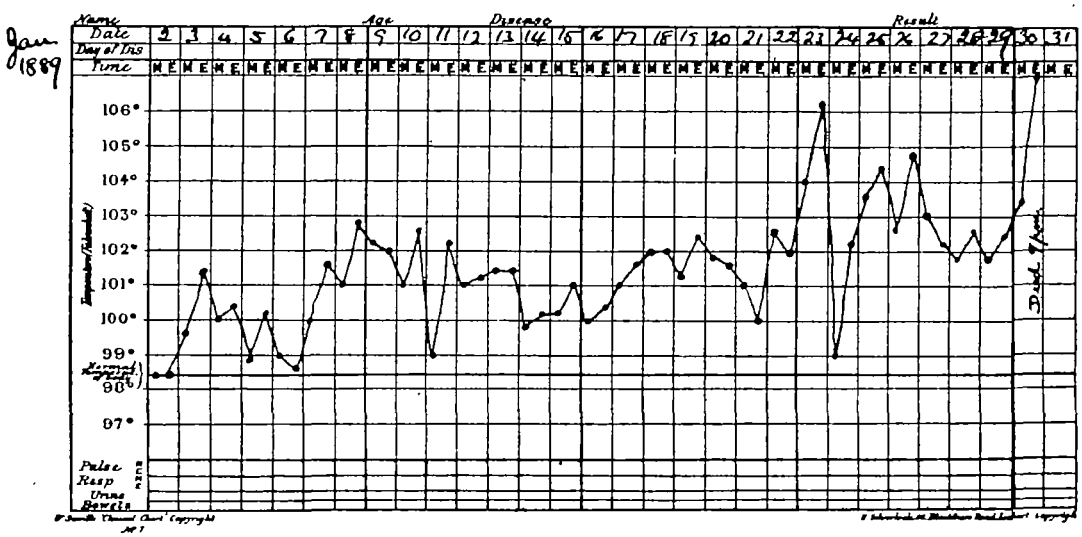

FIG. 7.—Temperature chart of C. M. (Gowers.)

disinclined to do anything. Her speech was noticed to become thick and indistinct, and occasionally saliva escaped from her mouth. On admission she was seen to be a heavy-looking girl, with mouth generally open and lower lip hanging down, and she was easily excited to laughter. Her tongue was found to be tremulous. She presented no other sign, and no evidence of organic disease of the central nervous system. Accordingly she was discharged after six weeks, but a month or two later involuntary movements of the limbs began, and progressed steadily, so that she was "always on the work." She used to be able to write well, but her writing rapidly deteriorated, and became almost illegible. She was readmitted to the hospital on January 2, 1889. On examination the striking feature was the more or less constant rhythmical tremor of arms and legs. As she lay in bed there was constant

regular movement of the feet with alternating contractions of flexor and extensor movements at the hips and knees. Similar rhythmical movements, consisting of alternating contractions of flexors and extensors, occurred in the arms. They could occasionally be stopped for a few seconds by voluntary effort. The lower extremities were rigid and in a state of contracture, and passive movements caused some pain.

The illness ran a steadily downhill course. The patient became emaciated, and fever developed (fig. 7); the tremors persisted, the rigidity increased. No sign of organic nervous disease was present, in the ordinary sense, except that the knee-jerks could not be elicited, presumably because of the rigidity. Death took place on January 30, 1889.

On pathological examination no definite morbid appearance was found in the brain or cord, but the liver showed an advanced degree of cirrhosis, strands of connective tissue enclosing nodules of varying size.

Both from the clinical and the pathological aspect the resemblances between this case and the previous one are of the closest. In spite of the grave and progressive nature of the nervous symptoms, no obvious lesion was found in the brain or cord to account for them, whereas an entirely latent and unsuspected hepatic cirrhosis was discovered. It is a curious feature of the disease that in all the recorded instances, as well as in my own series, with one exception (my Case 6), this cirrhosis has not revealed itself by any of the usual signs. Of this second case it may be remarked that the involuntary movements were definitely rhythmical and tremulous, more so than in the first case. It will be seen later that on this point the resemblance to the cases of the disease reported here for the first time is perfect. Although Gowers has described these cases as "tetanoid chorea," the involuntary movements were not constantly choreiform in the first case and apparently not at all in the second; while the epithet tetanoid is intended to specify a clinical appearance solely and not a pathological relationship.

The third case was recorded by Ormerod in the *St. Bartholomew's Hospital Reports* for 1890. The clinical notes were made without any knowledge of the above National Hospital cases; the resemblances, therefore, are all the more striking. The résumé of his case, given by Ormerod in the opening paragraphs of his paper, is here quoted in its entirety:—

Case 3.—"A boy, aged 10, previously healthy, is admitted with the following history. He has been getting ill gradually for three or four months. The

symptoms alleged are, in order of their development, weakness of right hand and arm, with cramped position of the fingers, soon followed by difficulty of speech. 'Drawing' of the face, then an unnatural gait. Speech gets worse: he seems 'silly'; has some difficulty in swallowing. Gait gets much worse. Lastly, some affection of left arm and hand.

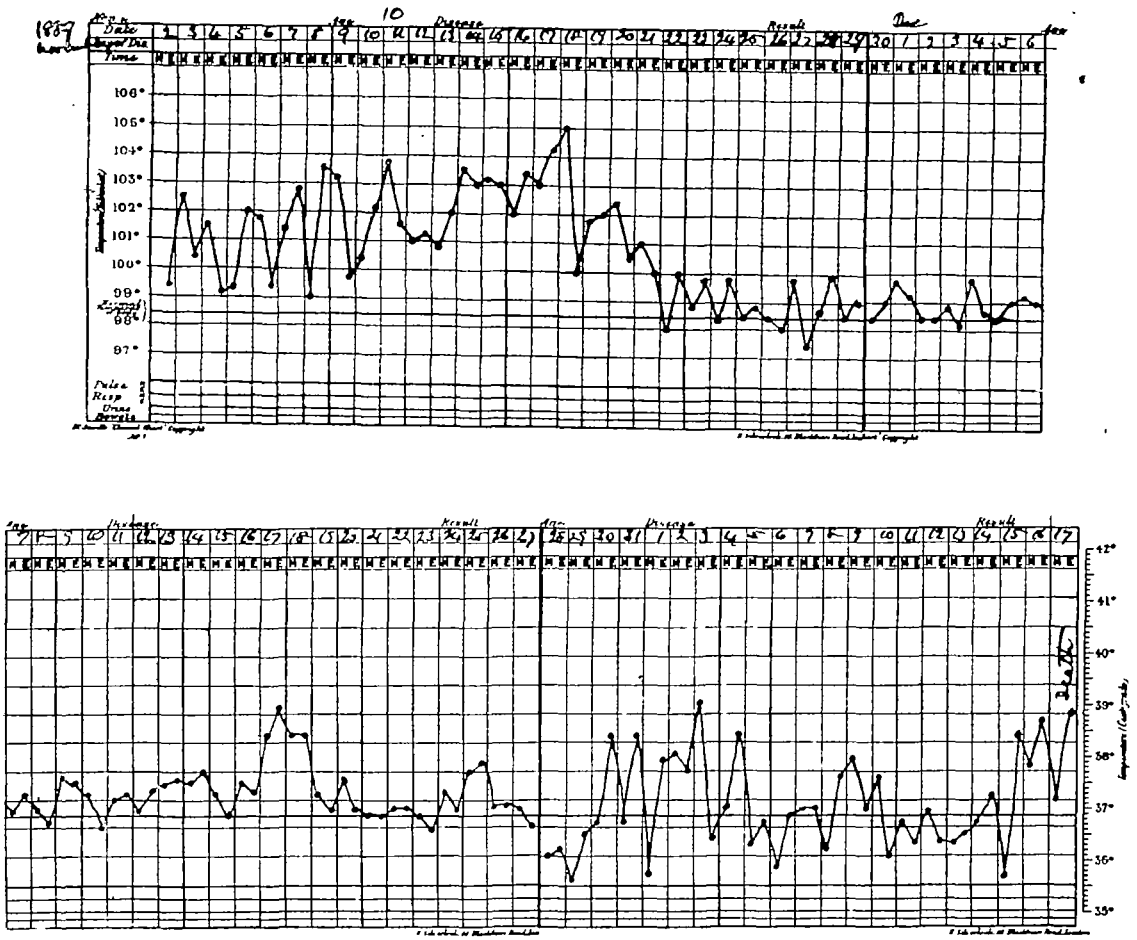

FIG. 8.—Temperature chart of W. S. (Ormerod.)

"The existence of these symptoms is verified after admission—a clumsiness of the right hand, with flexion of the thumb into the palm, and a tendency to rigidity at the knees, with uncertain, stiff gait, are noted. The only marked symptom, however, is inability to speak. He is not aphonic; he understands

all that is said to him, but says nothing, except on some rare occasions, when he speaks quite intelligibly. He has difficulty in protruding his tongue.

"In about three weeks paroxysms of pain, with contractions, begin in the left hand; he takes to shrieking. In ten days more he becomes very noisy, and apparently idiotic. The facial spasm becomes more marked. Nevertheless his symptoms are so vague, and apparently so much under his own control, that it seems probable that there is no organic lesion to account for them.

"This view, however, is negatived by the advent of more serious events; for, six or seven weeks from the time of admission, he becomes feverish (fig. 8); pulse very frequent; profuse sweatings. The legs become permanently drawn up, the right hand becomes weak, and like the left.

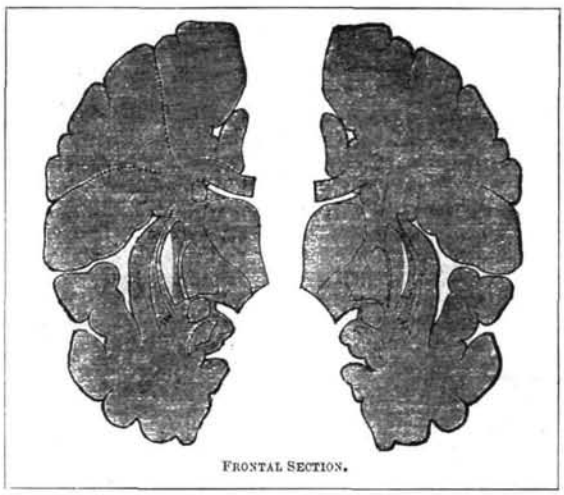

FIG. 9.—W. S. (Ormerod.) Bilateral softening in the putamen. (From *St. Bartholomew's Hospital Reports*, 1890.)

"His mental condition appears to get worse, and he lies howling all the day long. Finally, an acute bed-sore and signs of cystitis appear. In spite of a certain temporary remission, his condition gets worse, and the poor child dies, miserably emaciated, and his limbs distorted by contracture. Death takes place about four months from the time of his admission, and some seven or eight months from the commencement of his symptoms.

"*Post-mortem*, certain slight changes are found in the nervous system, but he has well-marked atrophic cirrhosis of the liver."

These changes in the nervous system are, as a matter of fact, of great importance. They consisted in a bilateral and symmetrical

area of softening, occupying the putamen or outer section of the lenticular nucleus, extending for about an inch in an antero-posterior direction, and involving chiefly its external part. The tract of disease on the right side was smaller in extent than that on the left. Fig. 9 is a reproduction of the drawing given in Ormerod's paper, and shows the appearances on frontal section at the level of the optic commissure. Microscopically in the affected areas were found closely packed lymphoid cells, in which a few vessels ran; the changes are supposed by the author to have been inflammatory. The spinal cord was perfectly normal. In the liver the characteristic appearances of cirrhosis were present, although the cells of the lobules were less degenerated than might have been expected, while amid the connective tissue growth bile-ducts were very numerous, and very prominent objects.

No one who peruses this brief sketch of these three cases, now more than twenty years old, can fail to appreciate their evident similarity. Indeed, they form a special group by themselves, for the cases published by Homén, as well as those of my own series, are, on the whole, more chronic and more slowly progressive. While, however, the latter may be in a sense less dramatic, yet they were none the less fatal, and their pathology is identical with that of the case that has just been described. These first three cases occurred in young people, beginning in an insidious way without apparent cause, and they were characterized by dysarthria, dysphagia, hypertonicity of the musculature, involuntary spasmodic movements, sometimes slow and tonic, oftener clonic and tremulous, contractures, and emaciation. The patients were obviously ill, with high, irregular fever, and great helplessness and weakness, yet both Ormerod and Gowers were struck by the fact of the occasional variability of the symptoms, and pointed out how readily and reasonably they might have been regarded, at least to begin with, as "functional"—i.e., hysterical. There was a curious disproportion between the clinical appearances and the actual objective signs of organic nervous disease. It may be remarked in this connexion that two of my own cases were at one time thought to be hysterical, and treated accordingly. Our ignorance of the symptomatology of extra-pyramidal motor affections, I believe, is the explanation of mistakes of this sort. Few doubt to-day that paralysis agitans is an organic disease of the nervous system, yet not so long ago its accepted place in the text-books was with neurasthenia and hysteria.

Before passing on to the next group—viz., those described by Homén

—it may be noted that Ormerod specifically draws attention to the following three points:—

(1) The presence of a cirrhotic liver in so young a subject.

(2) The absence during life of all ordinary symptoms of cirrhosis of the liver.

(3) The presence of severe and fatal nervous symptoms in a case where the nervous lesions found *post-mortem* were comparatively insignificant.

These problems can be better discussed after consideration of the results of the pathological investigations described farther on, which will materially aid us in this respect. There need be no occasion for embarrassment at the apparent absence of any definite positive findings in the brain in Gowers's cases, for in the first place the acute nature of the malady may not have allowed time for the development of changes that could be recognized, and in the second place histological technique has made considerable strides since the eighties of last century.

Under the title of "Eine eigenthümliche bei drei Geschwistern auftretende typische Krankheit unter der Form einer progressiven Dementia, in Verbindung mit ausgedehnten Gefässveranderungen (wohl Lues hereditaria tarda)," Homén, of Helsingfors, in Finland, published in the *Neurologisches Centralblatt* for 1890, the same year as Ormerod's paper appeared, and again more fully in the *Archiv für Psychiatrie* for 1892, an account of an apparently unique and unknown familial disease, which for various reasons, but in spite of the lack of positive evidence, he concluded might be a delayed manifestation of hereditary syphilis, a disease in which a sister and two brothers out of a family of eleven were affected, which ran a steady progressive course, and in each instance ended fatally. Its duration in these cases was three and a half, six, and seven years respectively. The clinical picture presented by the disease, and the pathological changes found *post-mortem* were not only identical in all three, but on all essential points offer the closest analogies to the description already furnished of the English group.

The following résumé of the cases is made from Homén's second paper [6], and includes the main features of this remarkable familial affection.

Case 4 (Homén's No. 2).—Alfred K. was born in December, 1866, and was in perfect health up to the age of 20. Without any apparent reason

he then began to suffer from a general listlessness and loss of appetite, and at the same time he seemed to become slow in his mental processes, and, generally speaking, more "simple." After about six months his gait was noticed to be stiff and uncertain; his articulation became indistinct, and tremor appeared in the arms and hands and became more and more pronounced. The stiffness, dysarthria, and tremor advanced to such a degree that the patient was ere long reduced to a state of helplessness.

On admission to hospital the chief symptoms and signs were as follows:—

The youth had a rather childish and stupid expression, the facial muscles being fixed and stiff; he seemed to understand everything that was said to him, but he scarcely ever spoke, and then always slowly; there was slight difficulty in moving the tongue. As he lay in bed the head was seen to have a more or less constant to-and-fro movement; the mouth was almost always open, the lower jaw tremulous; both arms and hands were in a state of contracture, the former being somewhat flexed at the elbows and the fingers flexed proximally but extended distally; they were very stiff, and passive movements were with difficulty impressed on them. The right hand was less affected than the left. A slow slight tremor of the hands from the wrists, in a radio-ulnar direction, was constantly observable, though occasionally it was more rotatory; a rhythmical tremor of alternating flexion and extension was often noticeable at the elbow. The lower extremities were also in a condition of contracture, and when the patient was put on his feet he required strong support. Even then the rigidity made progression almost impossible. Tremor of the legs was frequently noticed, especially when any voluntary movement was executed, chiefly consisting of alternating flexion and extension at knee and ankle. Voluntary effort always aggravated the tremor of the arms. There was some wasting of the muscles; sensibility was intact.

The patient's condition became steadily worse. Occasionally he spoke a few words distinctly, but gradually he became more and more inarticulate, as a rule simply giving vent to unintelligible sounds. The contractures increased, the tremors became generalized, and were sometimes observed in "attacks" which lasted for five or ten minutes and involved the whole musculature. Saliva escaped from the opened mouth. Attacks of clonic and tonic spasm spreading over the limbs, of a minute's duration, occurred during the last few weeks of life. Emaciation set in, bed-sores appeared, sphincter control was forgotten or lost, the patient passing everything beneath him. Difficulty in eating and swallowing increased, the temperature rose slightly, and on September 13, 1890, he died, having scarcely reached the age of 24.

At the autopsy the grey matter of the frontal convolutions was thought to be slightly atrophic or thinned, but the brain was of good size, weight, and shape; on horizontal section the middle zone of each lenticular nucleus was found to be softened and discoloured over an area of about 1 cm. in length and breadth. Slight sclerotic patches were discovered in the aorta and some of its main branches. The liver showed an advanced degree of cirrhosis.

Of the microscopical examination the following points will suffice for our present purpose. There was possibly some slight diminution in the myelinated fibres of the cortex in the frontal regions. While the pia mater was somewhat thickened, there was no small-cell infiltration, or only slight and scattered; the blood-vessels in the grey and white matter of the cerebrum were in many places irregularly thickened and hyaline or sclerotic in appearance; fine granules staining black with osmic acid were often noted in the vessel walls. The thickening seemed to be due mainly to the presence of fine granular masses of this description. While occasionally small round cells were found in the neighbourhood of vessels, they were few in number by comparison with the appearances in a brain of a general paralytic used as a control. The arteries of the middle cerebral distribution, lenticulo-striate, &c., were examined specially, and showed the same hyaline or sclerotic alterations; there were small collections of granular material, sometimes homogeneous-looking, sometimes with nuclei, lying round the elastic lamina, and occasionally bulging into the lumen of the vessel. The spinal cord was normal.

The only remark that need be made at this stage in reference to the microscopical findings is that the vascular alterations cannot be said to resemble a true endarteritis obliterans; in fact, Homén does not use the word in his description, and never refers to actual changes in the intima.

Case 5 (Homén's No. 3).—Wilhelm K. was born on August 8, 1870. He grew up a plump and healthy boy till the age of 12; but in the autumn of 1882 he began to complain of a general feeling of tiredness, and his memory and mental powers seemed to deteriorate. His gait, at the same time, became somewhat uncertain, and about a year later his articulation was noted to be defective. His arms became stiff to move, so that he had difficulty in making use of them, and simultaneously tremors developed in them, while the lower extremities began to become spastic or rigid. Very gradually contractures appeared, more especially at the knee and hip. After three or four years the patient was so helpless as to be bedridden; he scarcely ever spoke, and then only with difficulty and great indistinctness; his mouth was usually open and saliva dribbled from it.

On December 11, 1888, he came under the observation of Homén. It was noted that his speech was reduced to the enunciation of an occasional inarticulate and unintelligible sound, yet he sometimes managed to express some words with comparative clearness, especially if he was excited or disturbed. He lay in bed with his limbs in a state of contracture and drawn up, and yet by an effort of the will they could be very considerably extended, though not completely. Tremor was particularly well marked in the hands and arms, less obvious in the head and lower extremities. He passed his urine and stools into the bed. Emaciation was pronounced. The pupils reacted to light; cutaneous reflexes were present, but the tendon reflexes could not be tested

because of the contractures. Some small bed-sores appeared. The patient gradually sank and died on October 17, 1889, aged 19.

At the autopsy a horizontal section through the hemispheres showed that the optic thalamus, caudate nucleus, and internal capsule were perfectly normal, whereas symmetrically placed in each lenticular nucleus was an area of softening and degeneration that had resulted in the formation of a cavity. This cavity was about 3 cm. long and spread downwards and backwards to the lower extremity of the nucleus. The tissues round it were somewhat softened. Rather more than one-half of the nucleus, in breadth, was involved in the lesion. No other pathological change was visible to the naked eye. A few small sclerotic patches were found in the aorta, more particularly in its abdominal portion. The liver was in a condition of advanced cirrhosis.

Microscopically the blood-vessels of the brain were in some places irregularly thickened by the presence of granular or homogeneous masses between the membrana fenestrata and the intima; this granular change was apparently of a fatty nature in some instances, in other places it seemed to be more definitely cellular. Other blood-vessels seemed to be widened. Small round-cell vascular infiltration was almost completely absent.

Round the diseased area in each lenticular nucleus the tissues were degenerated and infiltrated to some extent with cells; but no microscopical alterations were discoverable in the other basal ganglia or in the internal capsule. The spinal cord was normal.

Case 6 (Homén's No. 1).—Anna K., the eldest member of the K. family, was born on July 26, 1862. She was a perfectly healthy child and girl, who never suffered from any special illness, and who had menstruated regularly at a normal age.

Towards the end of the year 1882, when she was 20 years old, identical symptoms to those from which her brothers had suffered appeared in her case—viz., headache, tiredness, loss of appetite, weakness, and impairment of memory. A few months later her walking became defective and her catamenia ceased. Then generalized stiffness of the trunk and limb musculature set in, and her speech became less distinct. Very gradually the arms and legs became contracted, the elbows, hips, and knees being the joints chiefly affected, and tremor developed in the arms and hands. As a result she became so helpless that she had to take to her bed. Dysphagia was a marked feature of the case. Her mouth was usually open and saliva escaped from it.

On August 29, 1888, she came into hospital. She lay in bed, helpless and apathetic, with a silly expression on her face; indifferent to her surroundings, she passed everything underneath her: she could not speak, as a rule giving vent to a few inarticulate noises from time to time, yet occasionally she appeared to wake up and then could articulate one or two words, though with difficulty. She died from inflammation of the lungs on October 19, 1888, at the age of 26.

On *post-mortem* examination the middle parts of both lenticular nuclei were found to be spongy and softened in consistence, and to be of a patchy greyish-yellow appearance. The liver was profoundly cirrhosed.

Microscopically the central portion of the lenticular nucleus, on each side, over an area of about 1 to 2 cm. long and 1 cm. broad, was discovered to be in a state of commencing disintegration, with disappearance of nerve-fibres and cells, and slight small-cell infiltration. A few small circumscribed "endarteritic" changes were noted in the Sylvian vessels.

Fig. 10 is reproduced from Homén's paper, and represents his third patient, taken about four months before the fatal termination. It conveys an excellent idea of his condition; the fixed smiling expression,

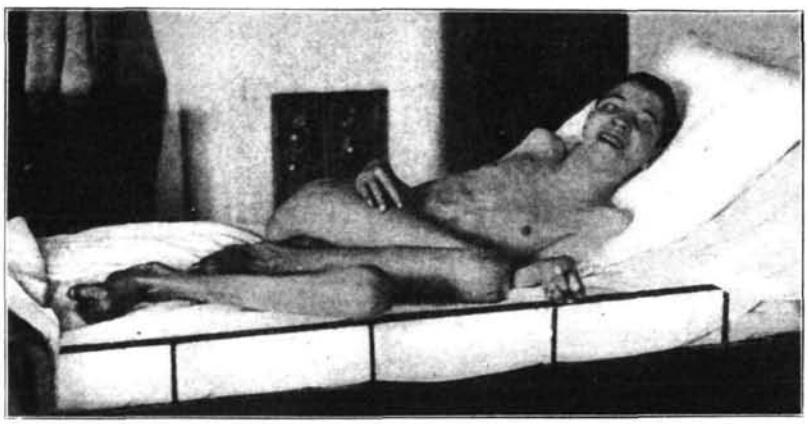

FIG. 10.—Wilhelm K. (Homén.) Note the fixed, smiling expression, open mouth, contractures, and some emaciation. (From *Archiv f. Psychiat.*, 1892.)

open mouth, emaciation, and contractures of arms, hands, feet and legs are well shown.

Such, then, are the three cases observed and described by Homén, which form a clinical picture of so definite a type that it is difficult to imagine how anyone familiar with the author's publication could fail to diagnose the condition if occasion arose. We can only conclude either that the paper has been lost sight of, or that the affection is characterized by considerable rarity, for no other instance of the disease, seemingly, has since been recorded—i.e., during the last twenty years. Reference will be made at the end of this chapter to Anton's case, published in 1908. While it presents certain resemblances to the cases under discussion, I am not convinced that its inclusion in the series is justified. The resemblance of Homén's group to the other three is very intimate. If the duration and the fever are excepted,

there is little else in which the two sets of cases differ. There is the same insidious onset, without apparent cause, in young people who have always enjoyed good health, the same steady progression of symptoms, until the patient is bedridden and helpless; the same dysarthria, involuntary movements, rigidity and contractures; the same emaciation and fatal issue. It is interesting to note that Homén was struck by the odd way in which the patient was able to articulate at one time better than another, as also by the fact that, in spite of contractures, there was often still a fairly wide range of voluntary movement if an effort was made. From the negative standpoint, the absence of ocular and pupillary symptoms, of loss to sensory tests, of definite alteration in the reflexes, beyond the difficulty in eliciting the knee-jerks owing to the muscular condition, and of impairment of "le langage intérieur," may be specified. On insufficient grounds, in my opinion, Homén came to the conclusion that he was dealing with one of the manifestations of syphilis hereditaria tarda, although he could obtain no parental history of syphilis, nor did any of his cases present unequivocal syphilitic stigmata. From the pathological point of view, moreover, his descriptions do not suggest syphilitic endarteritis. As there are no illustrations of any of his prepared material, we must judge to the best of our ability from the textual evidence. This evidence will be examined in a subsequent chapter.

Towards the end of his paper Homén declares that the clinical phenomena find a complete explanation in the results of the *post-mortem* investigations, but if his correlation of the two is scrutinized it is found to be open to considerable criticism. The tremors and rigidity he attributes to "cortical irritation" ("Corticalreizung"), as also the contractures, though probably in the later stages of the affection the nutritional element also entered into the causation of these; the difficulty in speaking and in swallowing, the open mouth and sialorrhœa are, in his opinion, all dependent more on "general intellectual deterioration" ("allgemeine Intelligenzabnahme") than on any local factor, and similarly with the incontinence of urine and fæces.

It is evident that he assigns more significance to the slight diminution in the myelinated fibres of the frontal region ("unbedeutende Verringerung myelinhaltiger Fasern"), the slight changes in the cells of the cortex ("geringe Ganglienzellenatrophie"), and to the scattered and irregular alterations in the cerebral blood-vessels, than to any other pathological defect. In spite of the fact that all of his cases were found

to have bilateral lenticular softening, he does not refer to it specifically in such a way as to show that he attributes any of the clinical phenomena to its presence. There is no hint of any special importance to be attached to it, no reference to the association of dysarthria and involuntary movements with disease of the basal ganglia, no distinction drawn between pyramidal and extrapyramidal motor disturbance. The remarkable problem of the association of cirrhosis of the liver with degeneration of the lenticular nucleus, as opposed to other basal nuclei, is apparently not mentioned. No one who is interested in the disease will undervalue the splendid contribution of Homén, but the essential and fundamental features of the affection must be interpreted in the light of more modern knowledge of cerebral physiology.

Reference has already been made more than once to an article by Anton, which appeared in the *Münchener medizinische Wochenschrift* for 1908, under the title "Dementia choreo-asthenica mit juveniler knötiger Hyperplasie der Leber." In this communication Anton describes the case of a young girl, aged 14, whose development was very defective, as she corresponded in size to a child of 8, and who had always been weak and easily tired. In her early years at school she had been noted for "making faces," inattention, and unmannerly behaviour, especially at meals. Thereafter her gait gradually became stumbling, her control over her limbs ineffective; she let things fall out of her hands, and her handwriting deteriorated. When she came under observation it was remarked that she stuttered; involuntary choreiform movements occurred, interfering with voluntary acts; her gait was ataxic. The reflexes were increased. Glycosuria was present. Her mental condition varied very much; she seemed facile and simple, but tired readily and then became uncommunicative. Later, her mental and physical condition became definitely worse. Her speech became dysarthric, she kept her mouth open, and often had attacks of impulsive laughter; her limbs sometimes trembled, but amorphous and inco-ordinate movements were more frequent. Mentally she degenerated profoundly, at length becoming definitely demented. Towards the end convulsive attacks occurred, with conjugate deviation of the eyes to the right. She died from heart failure.

At the autopsy the first left frontal convolution, and part of the second, were found to be softened over an area extending almost from the frontal pole to a point about 2 cm. in front of the precentral convolution. The pons was atrophied. The right suprarenal was

atrophic in its lower third. The genitalia (internal and external) were infantile. The liver was typically cirrhotic, its nodules varying greatly in dimensions, and hypertrophied. On microscopical examination there was much thickening of cerebral blood-vessels, especially in the frontal regions, but also in the cerebellum. The softening in the left frontal lobe was a gumma. The putamen on both sides was softened, and the external capsule partially so. The anteromesial part of the optic thalamus was poor both in fibres and cells. Small-cell infiltration was noted, more particularly in the cerebellum.

This case is interesting from several points of view, and it presents certain analogies to the cases already mentioned, which need not again be specified. Pathologically, however, there seems to be no doubt of the syphilitic nature of the case; it must, therefore, be classified as congenital cerebral syphilis. The frank infantilism, the glycosuria, the complete dementia, find no counterpart in any of the other cases, or in my own. The case is of value, however, for this reason, that part both of the clinical and of the pathological features is in harmony with the findings in the other cases, especially Homén's, to which, indeed, Anton refers.

Such, then, is a brief sketch of all the hitherto recorded cases [1]

[1] In the course of further search through the literature, while this paper was in the press, I came across a case under the observation of Frerichs, of Berlin, in the year 1854—i.e., fifty-seven years ago. It is recorded in his classical Treatise on Diseases of the Liver, and will be found in the second volume of Murchison's translation, published by the New Sydenham Society in 1860, p. 60. There is no doubt in my own mind that this case is one of the acute variety of progressive lenticular degeneration, and the fact that the essential clinical features of the disease can readily be recognized from a description of nearly sixty years ago affords striking proof of the specificity of the condition. The following extracts will suffice:—

"Carl Zeppner, a peasant's son, aged 10, was admitted on June 1, 1854. Up to a year before admission this boy had enjoyed good health, and in bodily and mental development had not been behind other children of his age. After bathing on one occasion, when he had been violently plunged by his companion with his head under the water, and kept there for some time, he complained of headaches and lassitude, became oblivious, began to stammer and to speak slowly and with difficulty, and gradually lost the power over his extremities. He often kept his bed for days on account of weakness; and when he wished to use his limbs, they were thrown into violent tremors. In other respects, his intelligence was not impaired, and his sensibility not diminished. Since Christmas he had completely lost all power of speech, and had been unable to swallow any solid food. . . .

"On admission, the boy appeared somewhat emaciated, but in other respects there was nothing else of an abnormal character to be observed in his external appearance. He was unable to stand or sit upright, or to hold anything in his hands; all movements were possible, but were performed very slowly and awkwardly; the sensibility was unaffected. His countenance exhibited an air of indifference, and failed to express either pain or pleasure; when the boy was told to distort his features, scarcely perceptible movements of the muscles of the face ensued. . . . The mouth opened slowly and incompletely. The tongue, which appeared somewhat flattened, but which was in other respects normal, was seized with a feeble tremor when the patient was ordered to move, or protrude it, or speak; the prick of a needle, however, could be felt in both halves of the organ. . . . The patient could swallow nothing but liquids, and even these with difficulty. . . . From time to time the difficulty of deglutition increased, and at the same time the movements of the extremities were imperfectly performed. . . . "

of the disease which I propose to call "Progressive Lenticular Degeneration." They constitute a little known chapter in nervous pathology, and present problems which it will be the purpose of this monograph to attempt to elucidate.

Chapter II.—Clinical Cases.

In this chapter the clinical histories of four personally observed cases are given in detail. The pathology of three of them will be described in the next chapter.

The first case that came under notice (S. T., Case 1) was that of a patient under the care of Sir David Ferrier in the National Hospital, Queen Square, in 1905. At that time I was not aware of the cases which have been sketched in the previous chapter, but it was certain that S. T.'s case was one of a nervous disease which did not correspond to any familiar type. Sir David Ferrier considered that while it bore certain resemblances both to disseminated sclerosis and to paralysis agitans, it was quite distinct from either. A year later the patient whose case is No. 2 (D. P.) came into hospital under the care of Dr. Ormerod, and whenever I saw her I recognized that her condition was identical with that of S. T. (Case 1), who had been in the hospital a year previously. It was this case that supplied the clue to the mystery, for the patient died not long afterwards, and at the *post-mortem*, made by Dr. Stoddart, of Bethlem Hospital, and myself, an unsuspected cirrhosis of the liver was discovered. Gowers meanwhile had republished his two cases in the *Review of Neurology and Psychiatry* [4], and they at once threw the illuminating ray for which I had been waiting

An acute attack of what seems to have been dysentery supervened, and after a few days of fever, violent diarrhœa, delirium and convulsions, the patient succumbed.

"The body was emaciated, but there was no œdema. The muscular tissue was atrophied. . . . The cerebral membranes were much injected. . . . The substance of the brain was soft. . . . everywhere it contained much blood. . . . Nothing abnormal could be found in the substance of the brain. . . .

"The spleen was enlarged—6¼ in. long, 4½ in. broad, and 1 in. thick. . . . The liver was small. . . . Its surface was covered with nodules, varying in size from a pea to a bean, and similar formations could be found in its interior, where they were separated from one another by broad bands of areolar tissue. The consistence of the organ was tenacious and leathery."

The resemblance is perfect. The youth of the patient, his previous normal development, the onset of dysarthria, dysphagia, weakness of the limbs, and tremors; the later emaciation, slowness of muscular movement without paralysis in the strict sense, the expressionless face, the increasing dysphagia and anarthria, the absence of any symptoms referable to the liver, and the intact sensibility, form an unmistakeable clinical picture. In spite of the fact that during life the symptoms are exclusively nervous, the sole significant pathological finding is extreme cirrhosis of the liver. In view of the acuteness of the lenticular disease the cerebral lesions are no doubt mainly associated with the severe illness of the last week of the patient's life. The same explanation holds good in this instance as in the acute cases recorded by Gowers.

over the darkness that enshrouded the others. Case 1 was followed up without delay, and a year later the autopsy revealed what was fully expected—viz., cirrhosis of the liver and lenticular degeneration. Case 3 was the brother of Case 2, and from beginning to end he was under my observation; in his case also similar pathological findings were obtained at the autopsy.

Case 4, which I owe to the kindness of Dr. Tooth, is that of a patient (M. To.) who was under his care in the National Hospital for a short time in October, 1911. The patient at the time of writing is still living. The clinical picture which her case presents is exactly that of the other three personal cases.

Two other cases, Nos. 5 and 6, will be found in this chapter. Case 5 is that of a patient referred to by Gowers as the eldest brother of his own two patients: "He was in the National Hospital six or seven years before, and died from some form of paralysis at the age of 15." A little trouble taken in tracing the movements of the M. family enabled me to find the mother of these patients, an old but vivacious lady, aged 70, and from her lips this history was obtained, which therefore makes the story of the M. family complete.

Case 6 is referred to in Ormerod's paper as follows:—

"A boy, aged 13, was under the care of Dr. Gee (at St. Bartholomew's Hospital) with ascites, anasarca, enlargement of the spleen, and purpuric spots on the legs. . . It was noticed before he left that he walked very badly. Subsequently he was admitted to Queen Square Hospital, under Dr. Thomas Buzzard, for nervous symptoms, mainly consisting of contractions of the limbs. He died, and the only definite lesion found *post-mortem* was cirrhosis of the liver." This case has never been published *in extenso*, and I am able to utilize it to render the record as complete as possible.

Case 6 presents certain features which distinguish it from the others, and in fact it is not clear, as in Anton's case also, that it is one of identically the same disease, but the resemblances are sufficiently close to warrant its insertion. In any case it sheds light on the etiology of the condition by analogy, if not directly, and for that reason it appears to me valuable.

Case 1.—S. T. was born on October 19, 1878. She was the youngest but one of the following family of nine:—

(1) Female, born 1859, living and well.

(2) Male, born 1861, living and well.

(3) Male, born 1862, died in infancy.
(4) Male, born 1868, died of diphtheria at the age of 15.
(5) Female, born 1869, died in infancy.
(6) Male, born 1875, living and well.
(7) Male, born 1876, living and well.
(8) Female, born 1878, died in 1908, aged 29 (Case 1).
(9) Female, born 1881, died in infancy.

Family history.—The father died, aged 68, of appendicitis. He had always been a healthy man, but is said to have been "highly strung," and of a somewhat neurotic temperament. The mother died, aged 65, of cancer. There was no history of any form of venereal infection in the family.

Previous history.—The patient was always a perfectly healthy girl, the only recorded illness being diphtheria at the age of 5. Her catamenia began when she was 14, and continued regularly for a year or two; thereafter she suffered from a certain amount of dysmenorrhœa for some years, but at the age of 20 the periods became more regular again. She was a well-developed, active girl, and used to be an excellent swimmer. Her mental development was rather above the average; she was fond of literature, and at school was considered to be of an original turn of mind.

Present illness.—In 1899, when the patient was 21 years old, and during a sojourn on the Continent, she had an attack of jaundice, of about five weeks' duration, but further details as to this illness are not forthcoming. For some years thereafter she suffered at intervals from slight swelling of the legs, which used to be puffy round the ankles, and she "used to make dints in them with her fingers." There were no other symptoms, and she was never laid up or incapacitated in any way by it.

In May, 1904, when she was 25 years old, she went to live in Schwalbach, and while there it was noticed for the first time that her right hand shook a little as she was writing, and that her articulation was not as clear as it had always been. She began to slur her consonants and the ends of her words. She seemed quite well in her general health, and her friends were at a loss to account for the symptoms.

By September of the same year her condition had altered definitely for the worse. There was a change in her disposition: she became restless, and appeared "unable to settle to anything," and it was remarked how easily she was provoked to laughter, the most trifling incidents causing her to smile spasmodically. The tremor became much more pronounced; it was noticed on both sides, and in the arms as well as the hands and fingers. Her speech became more slurring, and a certain slight difficulty in swallowing developed.

At the end of the year she was seen in consultation by Sir David Ferrier, who was at once struck by the curious appearance of the patient, her almost silly smile, her more or less constant tremor, and a certain fixity of expression, which led him to wonder whether he might not be dealing with a case of incipient paralysis agitans. Examination convinced him that there were no signs of organic disease of the central nervous system, in the ordinary sense;

there was no nystagmus; the reflexes were normal; a double flexor response was present. Accordingly he sent the patient into the National Hospital, Queen Square, for further examination and observation, on February 24, 1905, in the twenty-sixth year of her age.

She remained in the hospital for almost two months, and during this time was repeatedly examined. At no time during her stay were any of the accepted signs of organic nervous disease present, so that more than once the suspicion that her condition was hysterical crossed the minds of those of us that examined her. Yet it soon became evident that the progressive nature of the disease excluded hysteria, and as disseminated sclerosis, another possible diagnosis, was not at all probable, the question of the exact nature of the disease was left open.

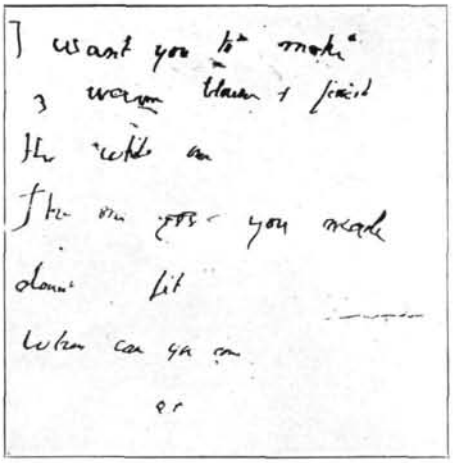

FIG. 11.—Handwriting of S. T. when in hospital.

The clinical picture which the patient presented was very striking. With a perpetual smile on her face, her mouth open, her limbs shaking, she moved slowly about the ward, often making very personal and apposite remarks about her fellow-patients; at other times she kept her bed, unable or refusing to speak when urged to do so. Her mental condition was curious; she showed an abnormal cheerfulness incompatible with the serious nature of some of the other symptoms: sometimes the expression on her face was fatuous, or silly, at other times she evinced considerable interest in things that would appeal only to an educated mind. She told me, for instance, that she had been learning Norwegian, and that when opportunity arose she intended to pursue her studies in that language. As for the dysarthria, so marked a feature of her case, there was no word which she could not pronounce more or less distinctly on different occasions, yet she was frequently unable to pronounce test words, and often her speech after a minute or two became simply unintelligible.

There was sometimes distinct difficulty in swallowing, but this symptom also was characterized by variability. Her handwriting was almost unreadable (fig. 11) owing to the constant tremor of her extremities—a quick, fine, rhythmical tremor which sometimes seemed to vary with the attention paid it, but at other times was unmistakeably of organic type, increasing with muscular effort. It was always well seen in the finger-nose test. The legs were affected with a similar tremor, also more noticeable during muscular effort. Her gait was usually slow and uncertain; her muscles were weak in proportion to their development, but there was no voluntary movement which the patient was unable to perform. The musculature, on the other hand, showed a slight degree of stiffness, especially in the fingers, which were constantly extended distally and flexed proximally.

In spite of treatment the patient lost weight while in hospital, and left on April 19, almost in the same condition as when she entered it; if anything, a little worse.

In the summer of the same year (1905) her increasing weakness and the possibility of her requiring nursing care for a lengthy period caused her friends to procure her admission as a voluntary boarder to the Holloway Sanatorium, Virginia Water. Here she remained for about two and a half years.

During that time the progress of the disease was slowly but steadily downwards, yet for a long time her general nutrition was satisfactorily maintained. From the careful notes of Dr. Sheila Ross, under whose more immediate care the patient was during her stay in the sanatorium, one or two excerpts will suffice to indicate the steps by which the illness progressed.

"August 17, 1905.—The hands are falling into a condition of contracture. The fingers of the right hand are flexed at the metacarpophalangeal joints while the phalangeal joints are extended, the terminal phalanx is hyperextended, especially in the third finger. The tongue is protruded with some difficulty, but is not tremulous. Patient walks unsteadily and turns with some difficulty, there is well-marked tremor in the legs, more particularly when she is fatigued. It is not easy to understand patient's conversation. Her manner is childish, but this is accentuated by her habit of using as few words as possible in conversation, owing to her difficulty of articulation.

"August 31.—The tremors are more marked in the right limbs than in the left. Sometimes they are severe.

"October 25.—The patient now spends almost the whole day on a couch, as her gait is very uncertain. Swallowing becomes more difficult, and she is occasionally dirty, especially in the morning; for the first half-hour after waking she seems stupid, incapable of emptying her bowel or her bladder, and as a result is sometimes wet and dirty. All the deep reflexes are normal; there is a double flexor response. The pupils react well to light.

"January 3, 1906.—Patient's gait is feeble and stiff; her limbs are in contracture and rigid. Speech is very defective; she usually spells out words on a card instead of speaking, but occasionally, if suddenly asked a question, she responds in a few words readily. Saliva dribbles constantly from her mouth,

and swallowing is very difficult. The coarse tremor of the right hand has increased, and on the left side tremor and contractures of the fingers are more noticeable. Patient menstruated last month.

"April 21.—Mentally she is very self-absorbed, frequently calling the nurses to her, and annoyed unless their whole attention is given to her. She can walk a little, on her toes chiefly, if supported by two nurses. In spite of the severe dysarthria she occasionally brings out a few words fairly smartly. Her physical condition is good.

"October 27.—When making any muscular effort saliva dribbles from her mouth and she appears to be unable to swallow it. She has menstruated again."

In view of the conclusion I had by this time come to, that the case was one to be relegated to the category of Gowers's so-called "tetanoid chorea," in other words, that it was a case of lenticular disease associated with cirrhosis of the liver, I took an early opportunity of going down to Virginia Water to examine the patient, whom I had not seen for about two years, for myself. I am deeply indebted to Dr. W. D. Moore and Dr. G. W. Smith for their kindness in affording me every facility in this connexion.

I saw her on March 14, 1907, when she was about 28½ years old, and made the following notes at the time.

The patient looks remarkably plump and well; she is exceedingly sunburnt, and gives an impression of good health. She is able to get up daily, and walk a little, only a few paces, but she can neither dress nor feed herself. She takes an intelligent interest in what is going on, recognizes her friends and visitors, her nurses, the doctors, and often endeavours to speak, but never with any persistence. She knows quite well when she is physically comfortable or the reverse; her disposition is more than ever facile, almost childish; she never cries, but, on the other hand, laughs on the slightest provocation, in fact without any provocation. Her features are usually fixed in a broad smile, showing most of her teeth. Her mouth is always open, her lips retracted, her jaws apart. (Compare figs. 12 and 13.) Saliva escapes from her mouth. She looks, at a first glance, and until one begins to examine her carefully, a semi-imbecile, living in a restricted microcosmos of her own. It is soon apparent, however, that the impression first conveyed is erroneous.

She recognized me at once, although we had not met for two years, and proceeded to spell out my name correctly on her alphabet, her fingers and forearm in a violent tremor the while. Her attention and memory were unexpectedly good; she proceeded to remind me of incidents that had happened during her stay in the National Hospital, and even of one or two of her former fellow-patients. It is true that her means of conveying to me what was in her mind were not particularly effective, but the defect was solely one of execution. During the whole of my examination she never failed to appreciate

what I requested her to do, and obeyed to the best of her ability. She did not complain of anything, she did not suffer from headache or giddiness.

SPEECH.

There is, to all intents and purposes, a condition of complete anarthria in her case. She never speaks at all under ordinary circumstances, preferring to use her alphabet, at which she is an adept. When she spoke on my request, what she said was unintelligible. I could not catch a single word. As her mouth was fixedly open, her lips and tongue stiff and almost immobile, the sounds seemed to come directly from her throat; it was curious to see her "speaking" when her face remained completely motionless. I was told, however, that sometimes when the patient seemed quite at her ease, and was not consciously making an effort, the articulation improved a little and some words could be distinguished.

There is neither word-blindness nor word-deafness. Writing is impossible.

FIG. 12.—Photograph of S. T. before the onset of the symptoms of progressive lenticular degeneration.

CRANIAL NERVES.

Vision is good. There is no restriction of the visual fields. The optic discs are normal. The pupils are regular and equal, of medium size, and react well to light and on accommodation. All ocular movements are good in range and free in all directions. Convergence is quite good. The patient,

however, is unwilling or unable to sustain any of the movements for longer than a few seconds. It is noteworthy, too, that when left to herself her eyes "dance" slightly before her gaze comes to rest on a given object. On testing her, however, there is no nystagmus in any direction.

The corneal reflex is present on both sides. There is no impairment of sensation over the face. The muscles supplied by the motor fifth contract well; she can close her jaws, and bite voluntarily, but the movements are

FIG. 13.—Photograph of S. T., taken at Virginia Water. Characteristic appearance of face and upper limbs. Compare with fig. 12. [For this photograph I am indebted to Dr. G. W. Smith.]

certainly slow, and she appears incapable of sustaining the effort, for her jaws open again almost as soon as they are closed. She cannot move her inferior maxilla well from side to side.

The ordinary expression of the patient's face is well seen in fig. 13. There is a spastic smile which is rarely relaxed, and is often aggravated into a spasmodic laugh. The upper part of the face moves well on volition; the orbicular muscles of the eye contract; the patient can wrinkle her forehead, frown,

&c., satisfactorily; the lower part of the face, however, is almost immobile; she cannot whistle, cannot purse her lips up, cannot blow out her cheeks. She can bring her lips together slowly, but the movement is not sustained.

There is considerable difficulty in swallowing, the food escaping from the corners of the mouth, or remaining on the tongue. Sometimes choking results. The palate moves well and symmetrically on phonation. It also moves when the fauces are tickled.

The muscles supplied by the eleventh nerve are very hypertonic, but the patient is able to turn her head to the right or to the left slowly.

The tongue is thin and looks atrophic; it is narrower in its middle part, relatively, than at the anterior part; it is slowly protruded with considerable tremor, but there is no tremulousness or fibrillation of the surface, nor is it puckered or fissured.

MOTOR SYSTEM.

The general muscular nutrition is fair, but there is some slight general wasting of the muscles; the small muscles of the hands are thin, more particularly perhaps on the left side. The arms as a whole are thin.

(*a*) *Tone.*—The examiner is at once struck with the generalized hypertonicity of the muscles of the neck, trunk, and limbs. It is more pronounced in the upper than in the lower extremities. As a consequence, passive movements are accomplished with some difficulty. Thus, if the arm be passively flexed at the elbow the tone of the triceps is such as to give the observer a sense of considerable resistance, and a similar phenomenon occurs when the arm is passively extended. The same thing may be observed almost at any joint. The neck muscles are very rigid; even when the patient lies down the sternomastoids are not relaxed. On passive movement the lower extremities feel very stiff. Direct muscular excitability is increased.

(*b*) *Power.*—Voluntary movements are greatly hindered by the spasticity. Yet the patient can by a voluntary effort flex and extend at all joints, can abduct and adduct at hip and shoulder, can rise to a sitting position with difficulty, can move fingers and toes. The movements which are least good are those at joints where contracture is most marked—viz., at elbows and fingers more particularly. The leg movements are relatively better than the arms. The actual power of the voluntary movements is certainly below the normal. They can be easily resisted by the examiner. There is, however, no paralysis anywhere.

(*c*) *Contractures.*—There is definite contracture of both biceps muscles; the long flexors in both forearms, specially the right, are in contracture; the left hand has adopted the interosseal position of paralysis agitans; on the right, the forefinger and second finger are extended and the thumb opposed to them; the other fingers are flexed into the palm (fig. 14). The terminal phalanges of the left fingers are hyperextended. In the legs there is some contracture at hips and knees, and the feet incline to the position of equino-varus. By careful

passive movement, however, it is possible to overcome much, though not all, of the contracture. The segments of the limbs where it seems most established are the distal. It is a curious fact that, though the patient sits in a chair with the general attitude of a double hemiplegia with contractures, the attitude is not really fixed, for there is still considerable voluntary command over the muscles, and by an effort the limbs can all be straightened to a certain extent.

(*d*) *Tremor.*—Undoubtedly the most interesting feature of the case from the motor standpoint is the never-ceasing tremor. Whether the patient sits in the sun or lies in bed she exhibits tremors of the whole body that seem

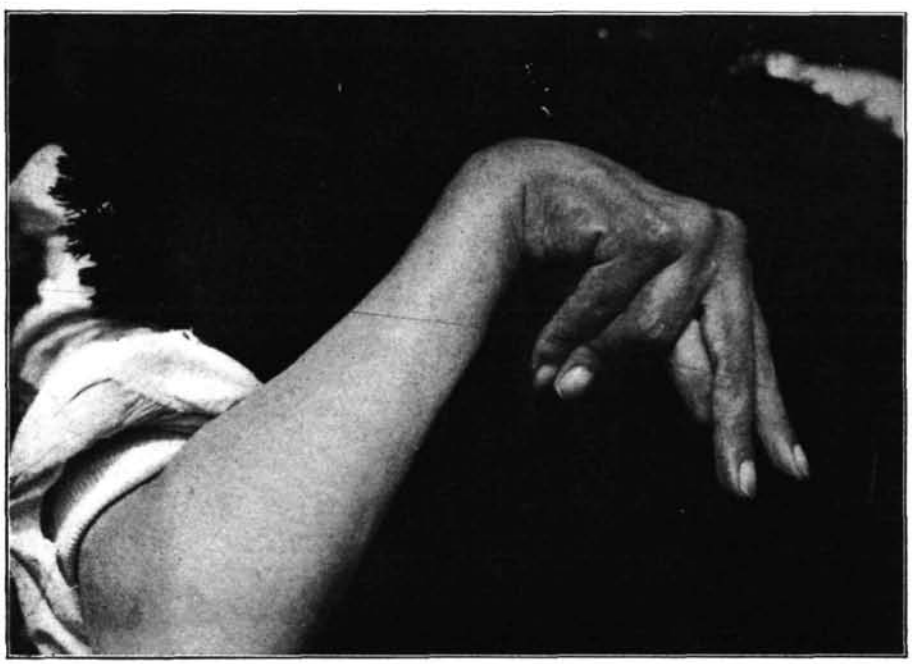

FIG. 14.—Right arm and hand of S. T., showing contractures, and resemblance of hand to that of paralysis agitans. (Exposure $\frac{1}{1000}$ sec., to obviate effects of constant tremor.) For this photograph I am indebted to Dr. G. W. Smith.

interminable. Even though she appears to be in a state of rest—i.e., well supported at all joints—the tremor never disappears. It is at once aggravated by any volitional effort, however slight, and it is made almost violent in such tests as the finger-nose test. It is particularly well seen when the patient endeavours to pick out letters on her alphabet.

In type it is usually quick and rather coarse—i.e., through a range of not less than 1 in. (2·5 cm.). Often the excursion increases considerably. The tremor consists of a true alternating rhythmical contraction of any given muscular group and its antagonists. In the arms the greatest movement is from

the elbows; the fingers and wrists are very stiff and move with the tremor from the upper arm. There is also, however, some interosseous tremor and slight tremor of the forefinger and thumb approaching to a rotatory type. The head moves with a slight to-and-fro tremor, and so does the trunk. In the legs the tremor is very well seen; even when they are at rest in bed it never ceases, and is at once aggravated by the slightest voluntary effort. The chief movement is one of flexion and extension at the hip, knee, and ankle, through a fine range, which is greater for the ankle than for the hip. There do not appear to be separate movements of the toes. I could not cause the tremor to cease entirely by supporting the whole of the limb, but undoubtedly it could thus be diminished in degree. The involuntary movements are never choreiform or athetoid.

(*e*) *Co-ordination.*—There is no real inco-ordination to be made out, as the patient is able to move her limbs in any given direction that is not prevented by the spasticity. When put on her feet she tends to fall in any direction indifferently, not from ataxia, but from the stiffness of her musculature interfering with her ability to keep her balance. When put in an upright position on the edge of her bed she falls backwards in a lump, the attitude of her limbs not altering in the slightest.

(*f*) *Gait.*—The patient requires very strong support, and can then walk a few paces, on her toes at first, more or less, but she gradually gets her heels down. The movements are highly stiff, tremulous, and uncertain.

SENSORY SYSTEM.

The patient does not complain of pain or paræsthesiæ, and on examination with the usual methods (touch, pain, temperature, deep sensibility) no definite alteration can be established.

REFLEXES.

All the deep reflexes are difficult to obtain, no doubt because of the rigidity of the muscles. They are present, however, though not brisk, and apparently equal on the two sides.

The abdominal reflexes are diminished on both sides, left more than right. An extensor response is obtained on the left side, and a flexor response on the right. There is no ankle-clonus. If the foot be pressed up on either side, the rhythmical alternating tremor of flexion and extension does not alter appreciably.

There is usually some incontinence of urine; it is not constant.

During the rest of the year her condition deteriorated step by step. Yet there was still an element of variability in the symptoms, often noted in regard to sphincter control. The anarthria became absolute, the contractures increased, and the patient began to lose weight. The tremor persisted without any change.

During the patient's stay at Virginia Water she was examined on several

occasions especially from the point of view of the functions of the liver. Notwithstanding that we expected to find a cirrhotic liver *post-mortem*, there were no symptoms of the ordinary kind associated with hepatic cirrhosis. In particular, there was neither ascites, nor œdema, nor distended veins, nor was there ever any icterus, even of slight degree. The liver was not palpable below the costal margin; its dulness in the nipple-line on the right side appeared, if anything, to be somewhat diminished. There were no symptoms referable to the stomach; no indigestion or sickness.

On January 29, 1908, the patient left the Holloway Sanatorium to live with her sister. She was examined before leaving, but no signs of physical disease, apart from the nervous system symptoms, could be discovered.

During the spring of that year her nutrition began to fail considerably, and she became very much thinner; with this increasing emaciation the contractures seemed to become worse, and all the symptoms were aggravated. She was utterly helpless, dependent on others for everything, anarthric and dysphagic, but at the same time she remained quite clear mentally, suffered from no delusions, was able to understand all that was said to her, and to express her wants in a way that could be understood by those around her.

In July, 1908, she was taken to be by the sea at an English watering-place. On Saturday, July 25, she was suddenly seized with an acute attack of hæmatemesis, vomiting 4 to 5 pints of blood. On Monday, July 27, she brought up a further 2 quarts of blood, and, sinking gradually, died on Tuesday evening, July 28, 1908, aged 29, after an illness of rather more than four years' duration.

Résumé of the Clinical History of Case 1.

A young woman, aged 21, whose family history is negative, and who has never suffered from any particular illness, who has always been intelligent and physically active, suffers from an attack of jaundice of about five weeks' duration, the exact details of which are not forthcoming, and at intervals thereafter, for about two or three years, has occasional swelling of the ankles, without being in any way incapacitated thereby. Four years after the icterus, at the age of 25, she notices that her right hand shakes a little as she is writing, and her articulation becomes a little slurring. In the course of a few months her friends notice a considerable alteration in her general condition; she is restless, unable to settle to anything, easily provoked to laughter, constantly smiling and unnaturally cheerful. At the same time the tremor spreads to both arms and hands, her writing deteriorates, her articulation is definitely impaired, and she has some trouble in swallowing.

At the age of 26 she is examined by a neurologist, who can find no signs of organic disease of the nervous system, notes that there is no

nystagmus, and obtains a double flexor response. Nevertheless the condition is steadily progressive; the tremors are accentuated, the dysarthria and dysphagia increase, a generalized stiffness of the musculature reveals itself, and the fingers begin to assume certain attitudes of contracture. Her mental condition is one of facility; she is easily amused, and constantly laughing; her mouth is open and saliva occasionally escapes involuntarily. In spite of the vacant expression on her face her memory and perception are quite good; she has neither delusions nor hallucinations; she is very observant and often makes apposite remarks about those with whom she is associated. The symptoms are characterized by a curious variability; articulation and the power of swallowing seem sometimes to improve, and there is no true paralysis, in the sense that all voluntary movements can be carried out, though slowly.

During the next two years the disease slowly progresses. While for a long time bodily nutrition is well maintained, the other symptoms increase in severity. The features are fixed in a perpetual smile; the mouth is wide open and the sialorrhœa is more marked; the patient is anarthric and dysphagic; yet with voluntary effort the mouth can be slowly closed, the tongue slowly protruded, while the palate rises on the attempt to articulate; the pupils react briskly to light, ocular movements are free, and the optic discs are normal. The muscles become more and more rigid, the arms, and to a less extent the legs, fixed in attitudes of contracture, which can be to some extent, but not entirely, overcome by passive movement; as a result the patient has become peculiarly helpless; but again on volitional effort a considerable range of movement is still possible. The tremor is absolutely constant, often wide in range and severe in degree; it affects all muscular groups in the limbs, especially the distal groups, but includes also the lower jaw, head, neck and trunk. No sensory change can be detected; the deep reflexes are present without being exaggerated, there is no ankle-clonus; the abdominal reflexes are diminished, and the flexor response on the left side has changed to extensor, the other remaining as before. Defect of control over the sphincters, probably of central origin, appears.

Eventually emaciation sets in; the patient is reduced to a profound degree of helplessness, is in a state of contracture, speechless, incontinent; nevertheless her mental condition remains clear, she understands everything and endeavours to express her wants. An acute attack of hæmatemesis ushers in the end, and she dies at the age of 29, after

an illness of rather more than four years. With the exception of the initial symptoms nine years previously, there have never been either symptoms or signs referable to disease of the liver, but this is suspected during life and confirmed at the autopsy.

Case 2.—D. P. was born on March 6, 1887. She was the eldest of the following family of six :—

(1) Female, died March, 1907, aged 19 (my Case 2).
(2) Male, died September, 1910, aged 22 (my Case 3).
(3) Female, aged 21, quite well.
(4) Female, aged 18, quite well.
(5) Male, aged 17, quite well.
(6) Male, aged 13, quite well.

Family history.—The sole data of any possible importance are that the maternal grandfather became alcoholic in old age, and that a maternal uncle and aunt died of phthisis, the former at 35, and the latter at 28. There was no history of any nervous disease in the family ; no history of syphilis on the part of either parents, or of gonorrhœa. The mother had had no miscarriages. At the time of writing both parents are alive and healthy.

Previous history.—The patient as a child was healthy and well nourished, so much so that she was called " Dumpy " by her parents. She was even-tempered and docile, and there were no mental peculiarities to lead to a suspicion that she was in any way different from other children. She never suffered from any serious illness at any time. She went to school, after private tuition, at the age of 14, and gave exceptional promise of doing well. Although she was a well-set-up girl, she never had menstruated.

Present history.—About the summer of 1904, when she was at school, and aged 17, it was noticed that she became rather untidy in her dress, where formerly she had been scrupulously neat. At the same time she began to lose flesh rather rapidly, and to look somewhat delicate. Her writing, which had always been good, deteriorated, and became " spidery." This was because of some difficulty in controlling the fine movements of her hands, and because of a quick, tremulous movement of the fingers. She took to writing in pencil instead of ink, and failed to obtain the same number of marks at school as formerly. This condition was ascribed to overwork, and the schoolmistress allowed her to do as she liked. The condition was progressive, however, and in June, 1905, she was removed from school and her parents took her to live with them in Italy.

It was then noticed that articulation was beginning to fail ; there was a tendency for the lower jaw to drop, so much so that her parents would say, " Shut your mouth, D——," which command she would instantly obey, but in a short time the mouth was open again. A degree of general muscular weakness was observable, more particularly on the right side. It appeared to be " heavy " ; nevertheless the patient could walk as much as four miles without feeling tired. Yet there was an element of awkwardness in her gait

which had not previously been present. At the same time her hands became more tremulous, especially if she felt that she was being watched. Her conversation became simpler, less intellectual, more childish; "her younger sister had to be a mother to her." In October, 1905, she developed some delusions. She chanced to pick a grape in a vineyard and thought that she was therefore wanted by the police. She also imagined that her father was a prisoner of the Pope. This delusional state, which was accompanied by some motor excitement, only lasted for a few days.

All the symptoms, the tremor, weakness, dysarthria, slowly increased in intensity. At the beginning of 1906 she occasionally suffered from spasmodic bursts of tears. Once when asked to make a choice from some articles for a present she could only smile in a spasmodic, silly manner.

FIG. 15.—D. P. before the onset of the symptoms of progressive lenticular degeneration.

The patient not improving, she was brought to England in the beginning of May, 1906, and seen by Dr. W. H. B. Stoddart, of Bethlem Royal Hospital, who after careful examination considered the case a nervous and not a mental one, and sent her to the National Hospital. When Dr. Stoddart (to whom I am greatly indebted for valuable help in connexion with this case) saw her he noted the following points:—

She was a tall, well-built girl of dark complexion, with a profusion of dark hair reaching to her waist. There was some pigmentation or discoloration in various parts of the body, especially round the ankles. She was not anæmic, but she had obviously lost much flesh. The tongue was dry and coated with a brown fur, and the breath somewhat offensive, but the teeth were normal.

Her general aspect was striking. The mouth was almost constantly wide open and the face wore a perpetual smile. The hands and arms were affected with a tremor that varied greatly in intensity from time to time, sometimes coarse, sometimes fine and scarcely noticeable. Owing to weakness and stiffness of her muscles she tended to fall to the right when standing or walking, or even when attempting to sit upright in a chair. She was childish in her behaviour; she laughed many times during the course of examination, and did not appear to realize the gravity of her condition. Her memory was unimpaired, and perception was perfectly good.

FIG. 16.—D. P. (National Hospital, May 1906). Note how patient is leaning over to the right side.

On May 11, 1906, the patient was admitted to the National Hospital, Queen Square, under the care of Dr. Ormerod, where she remained for almost a month.

She was carefully examined on many different occasions. She presented a striking clinical picture, some idea of which may be obtained from fig. 16. With mouth open, wearing a perpetual smile, she walked about the ward, moving slowly and tending to fall to one or other side, usually the right; she made childish remarks about trifling things in language almost unintelligible because of dysarthria, slurring the consonants and curtailing the last syllables, yet it was odd how this speech-defect could occasionally be overcome by an effort of the will. Her general appearance suggested a degree of mental

defect which was not nearly so pronounced as a superficial glance might convey. As I sat by her bedside one day I said jokingly, "Why, you're just a little girl," to which she replied quickly and with little or no articulatory defect, "I'm not a little girl!" as though to impress me with the fact that her looks belied her. Her attention was poor; ophthalmoscopic examination was difficult because of her unwillingness or inability to keep her eyes still. Her spasmodic laughter was remarkable; on slight provocation the smile on her face would broaden visibly and a curious laugh, with no "tone" in it, would escape in bursts.

The expression on her face was often rather vacant, especially if the otherwise fixed smile relaxed. There were no defects in the domain of the cranial nerves. The pupils reacted briskly to light. The optic discs were normal, and there was no defect of ocular movement, in particular no nystagmus. Facial movements could be carried out voluntarily, but somewhat stiffly; she was unable to whistle, and when left to herself kept her mouth constantly open. The palate moved normally, and there was little actual difficulty in swallowing. The tongue movements were not well executed; it was protruded slowly, but came out straight.

All voluntary movements were good in strength and range. There was an increased degree of tonicity in the muscles, but no contractures at this stage. When the upper extremities were at rest little or no tremor was noticeable, but when the patient made any voluntary movement it became very marked—a coarse tremor of hands and fingers, about four or six to the second, through a range of 1 or 2 in. (2·5 to 5 cm.). It was well seen in the finger-nose test. The same kind of tremor was present in the legs. Very occasionally, as she sat up in bed, a similar tremor, but finer in range, was observed to affect the trunk. There was no muscular wasting.

In spite of the patient's volitional control over her musculature, there appeared to be a rather disproportionate motor helplessness. When left to herself she would fall or roll about; owing to a generalized stiffness she could not, or would not, use her muscles to help herself, or keep herself from falling. This is seen in fig. 16, if the vertical lines of the curtain at the back are compared with the oblique position of the long axis of the patient's body. Her gait was slow, uncertain, stiff; her feet were kept apart, yet she had difficulty in maintaining equilibrium.

Sensation was perfectly normal. All the reflexes, cutaneous and deep, were normal. A double flexor response was constantly obtained.

As the patient's condition did not improve, and because of difficulty in getting her to take her food, she was transferred to Bethlem Hospital, under the care of Dr. Stoddart, on June 6, of the same year, 1906, being then 19 years old. From that date, until her death the following March, I had many opportunities of observing the progress of the disease, of which the following notes will convey some idea.

For some time she had to be tube-fed, because she was apparently under the impression that her food was poisoned, but this idea passed off, and she

did her best to take food voluntarily. She had, however, the greatest difficulty in swallowing it, and a few days before her death the dysphagia was so complete that tube-feeding had again to be resorted to. It is worth remarking that even when the dysphagia was greatest some efforts at swallowing were executed more easily than others, and that the reflex was present throughout.

Up to the end of 1906 the spasmodic smile was fairly well marked, but during the last two months of life it gradually diminished, and the facies became characterized by a complete absence of expression. The lower jaw dropped still more; even during sleep the mouth was open.

The tremor of the extremities became increasingly severe: its excursion was sometimes as much as 3 in. (about 7 cm.). Towards the end the tremor of individual fingers was more prominent than ever; it was usually antero-posterior, but sometimes lateral, the rate being about four to six a second. The tremor of the legs and trunk persisted. Weakness of the limbs increased almost daily; as late as the beginning of January, 1907, the patient was still able to stand, though only with assistance, but thereafter her helplessness became so pronounced that she was kept in bed. After this, contractures of the limbs set in with rapidity; at the elbows, hips, and knees the limbs were drawn up. The spine became very rigid. For some months before her death she was unable to protrude her tongue. The weakness and tremor were throughout more marked on the right side. In spite of every effort to maintain her general nutrition the patient gradually became emaciated, but there was no local muscular atrophy, nor was there more general wasting of the musculature than could at first be accounted for by the continued rest in bed, but towards the end the emaciation became extreme. Sensation remained normal throughout.

The knee-jerks were moderately exaggerated; there was no ankle-clonus at any time. The abdominal reflexes were never abolished; they were obtained on February 27, four days before the patient's death. The plantar reflexes remained of the flexor type on both sides, although during the last three days of life some variability was noted. During the early months of the year some weakness of the anal and vesical sphincters set in, not, however, of local significance, in all probability; the patient usually indicated when she experienced a call to stool, and was, therefore, generally kept clean; but if, at the moment, there happened to be no nurse in the room, the dejecta were passed into the bed.

From the time when the patient went to Bethlem Hospital dribbling of the saliva was a prominent symptom. At first handkerchiefs were used as bibs, but eventually it became necessary to employ a large towel, so profuse was the sialorrhœa. It was a remarkable fact that during the last week of the patient's illness this flow of saliva entirely ceased.

On the evening of February 24 the temperature rose to 101·2° F., and sibilant râles could be heard in various parts of the chest. Two days later there was a patch of dulness at the apex of the lower lobe of the right lung. The temperature varied from 101° to 103° F. During the last two days the respirations

became somewhat hurried, and were accompanied by dilatations of the alæ nasi. The patient gradually sank, and died on the evening of March 3, 1907, being then 20 years old all but three days.

Résumé of the Clinical History of Case 2.

A girl, aged 17, in whose family history no factor of any pathogenic significance can be discovered, and with a clean bill of previous health, with the sole exception that she has never menstruated, is noticed to develop a fine tremulous movement of the fingers, so that her handwriting deteriorates, to lose flesh, and to fail somewhat in her school work, so that she does not obtain the same marks as formerly.

Some six or nine months later, her age being 18, it is found that her articulation is becoming defective, and that she tends to keep her mouth open. A general muscular weakness appears, and the tremor of the hands increases. Her conversation becomes simpler and rather childish, and she suffers from one or two delusions, which, however, do not persist.

Rather more than a year from the onset of the disease, the tremor, weakness, and dysarthria have become more pronounced. She has occasional attacks of spasmodic weeping, but as a rule her face wears a stiff, spastic smile, her mouth is always open, her limbs show a more or less constant rhythmical tremor, which increases with muscular effort, and she has great difficulty in maintaining her equilibrium, owing to a generalized weakness and stiffness of the musculature. She laughs at trifling incidents, and often, indeed, without apparent cause, but on careful examination and observation it is found that she is not in reality suffering from that degree of mental impairment which her appearance suggests. She presents no ordinary sign of organic disease of the central nervous system; the pupillary, cutaneous, deep and organic reflexes are all normal.

In about two years or less from the beginning of the disease dysphagia becomes evident, she seems to be very helpless, falling about, and unable to maintain her balance, her muscles are both weak and hypertonic, but there is no true paralysis, as all voluntary movements can be performed, though slowly. The tremors and dysarthria become extreme. In spite of her perpetual smile and silly appearance, her perception is good and her memory unimpaired.

During the next few months, and in the latter part of her twentieth year, the disease runs a downhill course. Saliva escapes from her open

mouth. The hypertonicity of the musculature increases, her face is fixed and expressionless, her weakness and helplessness are profound. Contractures appear at elbow, knee, and hip, the tremor of the fingers, arms, trunk, and legs becomes coarser in type and is often violent, the dysphagia and dysarthria are such that maintenance of the patient's nutrition is a serious problem, while her speech is unintelligible, and in fact she scarcely utters a single word. Examination shows that there is no involvement of the pyramidal system, for the abdominal reflexes are always obtainable, and a double flexor response is constantly noted. Sensation is intact, the ocular movements are free, and there is no nystagmus.

At length, emaciated and in a state of contracture, she dies from bronchopneumonia, aged 20 years all but three days, three years from the commencement of the illness. Notwithstanding the fact that the patient has been exhaustively examined on many occasions, there are never any symptoms referable to the liver, nor has she presented any signs that might be associated with disease of that organ.

Case 3.—E. P., the eldest brother of the patient D. P., whose case is No. 2 in my series, and the second member of the family in order of birth, was born on May 14, 1888.

Previous history.—With the exception of whooping-cough at the age of 9, the patient passed a normal childhood and boyhood. He was active and intelligent, and never had anything the matter with him. He went to school at the age of 12½ years, and had an excellent scholastic record. Here he remained doing exceedingly well till Easter, 1906, when certain symptoms unexpectedly appeared, to the surprise and distress of his relatives.

Present history.—During the spring months of that year, when the patient was almost 18 years old, he had been working very hard for an examination and broke down under the strain. He found he could not concentrate his attention on his work. He was keen on athletics and had been playing football all winter, but games had to be given up. An attack of motor excitement accompanied by hallucinations of hearing suddenly ensued, and he became unmanageable. On two medical certificates he was admitted to Bethlem Royal Hospital, on April 11, 1906.

These certificates contained the following statements: "The patient is very excited and emotional, says he is being influenced, willed, or hypnotized to do certain things, is quite sure that God is working a miracle on his behalf. Says he has heard God and the devil talking to him simultaneously, and does not know which voice to obey. Is frightened because, although he has been baptized, he is not now certain whether that has secured his salvation."

On examination at the hospital he was seen to be a tall, well-developed

young fellow with a dark complexion. He presented no symptoms of organic disease of the central nervous system. His speech was normal; there was neither rigidity nor tremor; the pupils reacted briskly; all cutaneous and deep reflexes were normal. The urine contained no abnormal constituents. On the day after admission he already appeared to be more rational and his temperament was noted as being bright and cheerful. He admitted that about ten days previously he had heard the voice of God speaking to him, but now thought it might have been a dream. Voices in his ears which he then heard he said might possibly have been those of other people in the building.

During the summer his condition gradually improved. At intervals he was subject to hallucinations, and at these times he became excitable and restless, laughing and crying alternately, and suffering much from insomnia. By the end of July, 1906, with the exception of these attacks, which lasted about a week at a time, he was more himself again, and from that time he improved steadily. He was so well that on February 5, 1907, he was sent to the Bethlem Convalescent Home at Witley, not having shown any symptoms for months previously. He was discharged recovered on April 3, 1907, and went out to Italy to his parents.

Although submitted to several careful neurological examinations by Dr. Stoddart, he never showed any sign of organic disease of the nervous system, and the diagnosis of exhaustion or toxic psychosis seemed entirely justified. A good prognosis was given.

During the summer of 1907 he was very well. He took long walks and climbs, being away for twelve hours at a time, and never gave cause for any anxiety on the part of his parents. He was quiet and reserved, it is true, but he always had been of a rather retiring disposition.

Towards the latter part of the year, however, when he was 19, a different group of symptoms made their appearance and progressed with rather alarming rapidity. He began to have difficulty in speaking and swallowing, and his mother noticed how constantly a thin stream of saliva used to escape from the corner of his mouth. Further, his hands became tremulous, and his handwriting became very bad. He did not complain of anything, had neither pains, headache, nor giddiness, yet in three months' time his whole condition had altered appreciably for the worse.

During 1908 the disease advanced steadily. The tremor became generalized, the dysarthria more pronounced, so that he rarely spoke at all, the difficulty in swallowing did not diminish, and he had a constant tendency to let his mouth open, sometimes widely, without apparently being aware of the fact. His limbs, more particularly the legs, became stiff and weak, but there was no paralysis in the ordinary sense of the word, as he could move them well enough, and could walk about without any assistance. He was sent to be under the care of Dr. Reymond, at Chexbres, near Lausanne, and in a letter from his father, dated November 13, 1908, from which the following passages are taken, I received some information as to the patient's condition :—

". . . . His main difficulty now is that he swallows badly and that his

articulation is very imperfect indeed. He is still troubled with an abnormal flow of saliva. Still, compared with his previous condition, I think there is improvement in each of these directions. When I saw him I certainly understood him better than some months previously, but articulation is most defective still. . . . As to his ability or inability to walk and stiffness of legs, of which you ask, I think there is some improvement. During the two days that I was with him we walked, and even climbed, a good deal, and it was I, not he, who always tired first. Dr. Reymond thinks that there is nothing wrong whatever with the boy's mental condition. Certainly in long and searching conversation, and in his various letters home, we never see the slightest sign at all of mental trouble. I do not think that I can say that the mind is equal to vigorous work. He reads a great deal, but does not ask for deep books. His

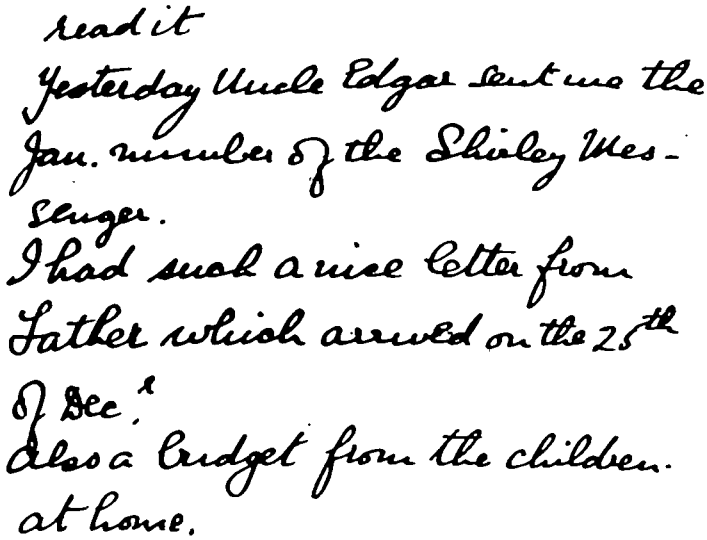
read it
Yesterday Uncle Edgar sent me the
Jan. number of the Shirley Mes-
senger.
I had such a nice letter from
Father which arrived on the 25th
of Dec.
Also a budget from the children
at home.

FIG. 17.—Normal handwriting of E. P.

memory seems exceptionally strong. He writes very badly, and, if possible, gets someone to write for him. But he sent us last week an eight-page dictated letter, sensible, bright, and full of interest, exactly reproducing his thought as he gave it. This may have been dictated at more than one sitting, but it certainly means that the boy is quite able to express himself upon all ordinary lines, and, further, that he managed, whether with or without difficulty, to make his amanuensis clearly understand, at his dictation, eight pages of matter. Of his own handwriting I send you a specimen herewith. [Compare figs. 17 and 18.] . . . He looks to me a little stouter. . . ."

During 1909 the illness progressed slowly but steadily in a downward direction, and at the beginning of 1910 it became clear that there could be only one end to it, and that perhaps not very far off. I cannot do better than

quote some sentences from a letter from the patient's father, dated May 27, 1910:—

". . . . I am sorry not to be able to give you a good report of E——'s progress. As far as I am able to judge, the mind is perfectly clear, and I think on the whole the lad is happy. But there is a very distinct and marked failure in physical strength. . . . The symptoms are very greatly aggravated since I last wrote to you. He seems to have lost almost entirely control of his motor nerves. The effect of this is that he cannot grasp, that he swallows with so great difficulty that it is a serious matter to get him fed, and his power of articulation is so very slight that one can hardly understand a single word he

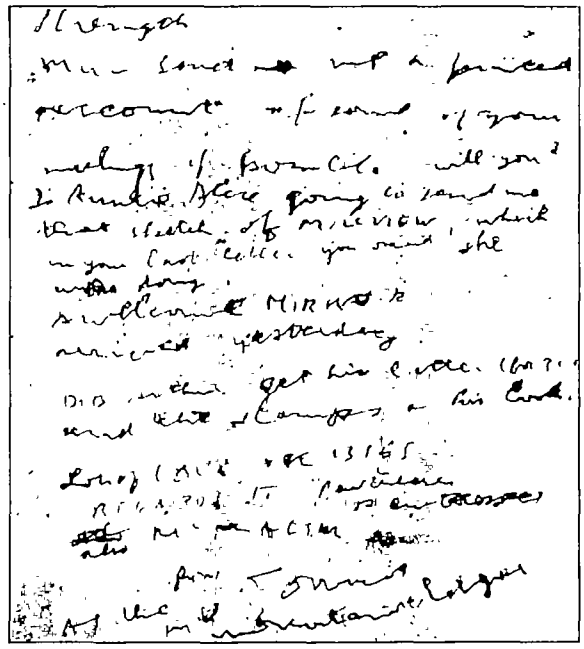

FIG. 18.—Handwriting of E. P. after the onset of progressive lenticular degeneration.

utters. Dr. Reymond has given him a kind of tablet with the alphabet in letters each about 1½ in. square, at which he tries to point, to spell what he wants to say; but in any attempt to indicate a letter with his finger, the trembling, I could almost say the vibration, of his hand is so violent that it has to be held and steadied before it can reach a desired letter. He has lost control in some measure of the physical functions of the body in a way which makes the care of him difficult for others. He is wonderfully patient and of a happy disposition, though one can see that he suffers very much, naturally, at not being able to express himself. . . . This fact of itself, you will note, proves a considerable measure of balance of mind. . . . E—— cannot now get his hand

anything like steady enough to write a stroke; the poor fingers, when he tries to hold pen or pencil, shaking, or rather swinging, with a swing of two or three inches, or even more. His limbs are somewhat emaciated. He is not now strong enough to walk many paces. . . ."

As the patient had not been seen by any neurologist since the onset of the symptoms of progressive lenticular degeneration in the autumn of 1907, it appeared to me desirable to investigate his condition for myself. Accordingly, an early opportunity was taken of paying a visit to the sanatorium where he was living, and the greater part of Saturday, June 4, 1910, was spent in examining him. The following description is based on the notes made at the time.

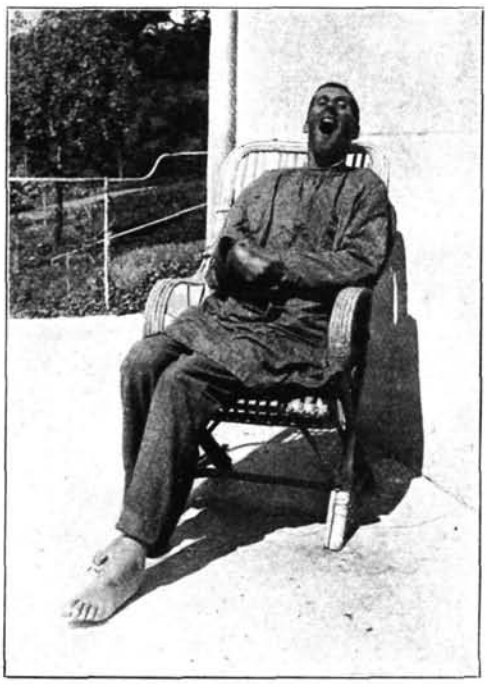

FIG. 19.—E. P. (June 4, 1910). Note mouth, contractures, tremor of the hands. (Exposure, $\frac{1}{170}$ sec.)

GENERAL AND CEREBRAL.

As I walked round the corner of the building and came upon the patient sitting in a lounge chair in the sun, the impression I received was one not easily to be forgotten (fig. 19). He was leaning back with a broad smile on his face, his mouth wide open and the saliva dribbling from it on to his chest, his arms and hands were in a state of contracture and drawn up, moving to and fro ceaselessly with a quick rhythmical tremor; his toes tapping the ground with a similar rhythm, his whole attitude one of vacant complacency.

If, however, this first impression was one of the utter helplessness of the patient, it was not long ere one perceived that it was to a certain extent erroneous. It is true he had apparently no idea who I was, although we had met several times previously, and he did not appear to show any signs of interest or recognition when I spoke to him of his mother. On the other hand, he evidently knew familiarly the various inmates and members of the staff of the place, and he could pick out with accuracy the various photographs of friends scattered about his bedroom.

His mental state was one of great facility; he was as docile as a child. He did whatever he was told to do, often with a brief, involuntary, explosive laugh. Aware of this mental condition, some of his fellow-patients would say, "Open your mouth, Mr. P.," and this he would at once do, to the accompaniment of bursts of laughter. He laughed constantly while he was being examined, yet when he noticed that one of the legs of my camera was unsteady he at once put out his left hand to hold it, though the movement was slow.

He read the English journals every day, and used his alphabet quite intelligently. He knew where everything was in his bedroom, or round about him, that was required for his use, although his gestures to indicate what he wanted seemed to me to be poor. Others, however, more familiar with him, could understand perfectly. He was hugely pleased with any little attention paid him; if his mouth were wiped he passed at once from his smile to his laugh. When his reflexes were being tested he burst into a loud "rire spasmodique," and I got a most distinct impression that he remembered that sort of thing having been done before. He was evidently acquainted with the use of all sorts of articles with which I tried him; he was, however, unable to do anything for himself, his movements being so very slow and laboured.

It was difficult to be sure whether he was correctly oriented in time; he appeared to be well enough aware of what was going on in his own little world. It was curious how quickly he noticed things; when I helped to dress him after examination he corrected me several times in my manner of doing it. He seemed quite happy and contented, and did not appear to have complete insight into his own condition. Nor could I interpret any of his actions or gestures as indicating that he suffered mental pain at being unable to express himself. He appeared to have little initiative or spontaneity, although, I suspect, this may possibly have been due to some consciousness of his helpless condition.

As for his general physical condition, he was tremendously sunburnt, but very thin. There was not an ounce of fat on his body. The outlines of the muscles and tendons were everywhere clean cut. The vertebral spines were very prominent. The face was comparatively well nourished. The genitalia were well developed, and there was a good deal of pubic hair. The feet were somewhat œdematous, and the ankles a little puffy, but this œdema could not be dimpled with the finger. There was no abnormality, however, of heart or circulation.

Perhaps the most striking feature of his case was his complete helplessness,

and the indifference bred of a knowledge of this. He sat in the sun in the chair, rolling over to one or other side if he lost his balance, the extraordinary hypertonicity of his musculature making the effort to recover himself almost useless. I found him, on one occasion, leaning right over the arm of his chair, the fixed smile on his face, apparently content to hang thus until he was found and put back in position. His indifference was sometimes remarkable. On several occasions he kept his mouth wide open long after I had asked him to open it; similarly he once kept his tongue protruded for several minutes. Occasionally the smile relaxed and the vacant expression became less obvious, but he never seemed to express any other emotion, and made no visible facial response when I gave him messages from his parents, or when I finally said good-bye.

SPEECH.

During the whole time we spent together he said only three or four words, of which two were, "I will." These words seemed to come from his throat, after the fashion of a ventriloquist, for there was no appreciable movement of lips or tongue. His anarthria was complete. So too, practically speaking, was his speechlessness; he made no effort in response to my urging him at least to attempt it. Nor did he appear distressed at this.

On the other hand, he used his alphabet with perfect correctness, spelling out such words as "doctor" without any difficulty. He appeared to be able to read quite well, and to understand what he read. Various drawings of familiar objects he recognized easily. He never once failed in the whole of the examination to perform correctly what he was asked to do—with the exception of the speechlessness—although, of course, the actions were very slow. There was no apraxia to be detected, and no agnosia. It struck me as affording a remarkable contrast, this *apparent* imbecility, compared with his quickness in appreciating everything the examiner did, or said, or asked. When I proposed going inside the house he at once tried to get on to his feet; when I asked for a towel he indicated where to find one; when I requested him to do this or that for the purposes of photography he co-operated with the greatest intelligence. Thus to apply the term dementia to his mental condition would be inaccurate. Writing was impossible.

CRANIAL NERVES.

Vision was good. The visual fields were normal. The optic discs (emmetropic retina) presented no visible abnormality. Ocular movements were good in all directions, and there was no trace of nystagmus. Sometimes the ocular movements seemed better sustained than at other times, but this was solely a question of attention. When the patient moved his eyes about of his own accord and not to command, it was noted that there was occasionally some unsteadiness in fixing an object; this, however, was only momentary.

The pupils were regular, equal, and of medium size; they reacted briskly to light, and contracted well on accommodation.

The corneal reflex was brisk on both sides. There was no sensory impairment over the face. The motor fifth muscles contracted well. The masseters contracted so that the patient could close his mouth, but the movement was slow and not well sustained, as the patient was in the habit of keeping his mouth widely open. Opening of the mouth against resistance was unexpectedly powerful. The whole of this musculature was hypertonic, and the patient had difficulty in moving his jaw from side to side.

Except when the patient's face was contracted into a broad smile, he had an utterly stolid, mask-like facies, the facial lines round his mouth being obliterated, and the latter simply an aperture in the mask; the lips themselves, however, did not hang much (compare figs. 20 and 21). Frequently he wrinkled his forehead and made other movements of the upper face, but his

FIG. 20.—E. P. in his school days.

mouth never moved except when he went off into the smile or laugh, which, it is true, occurred almost every minute. On attempting to whistle only a feeble contraction of the orbicular muscles was detected, and he was unable to make any sucking movements. When urged to show the teeth—i.e., to retract the corners of his mouth—he indulged invariably in a spasmodic laugh, so that it was difficult to gauge the amount of voluntary movement. He could wrinkle the forehead, frown, close eyes tightly, &c., quite well to order. When the muscles contracted into a smile it was always a stiff, tonic contraction, which did not relax quickly, and often remained fixed, one might almost say pinned, on the patient's face. The fact that the lips did not hang down showed the tonicity of the musculature.

Hearing was normal on both sides.

The palate moved well and symmetrically in the effort to phonate. The patient usually succeeded in saying "ah" very fairly. The palatal reflex was present on both sides. Swallowing was very bad indeed. He could not make the movement of swallowing on request. Water he swallowed in gulps, noisily, a great deal of it swimming about in his mouth and running out at the corners. He was unable to approximate his lips sufficiently to grasp the edge of the vessel adequately.

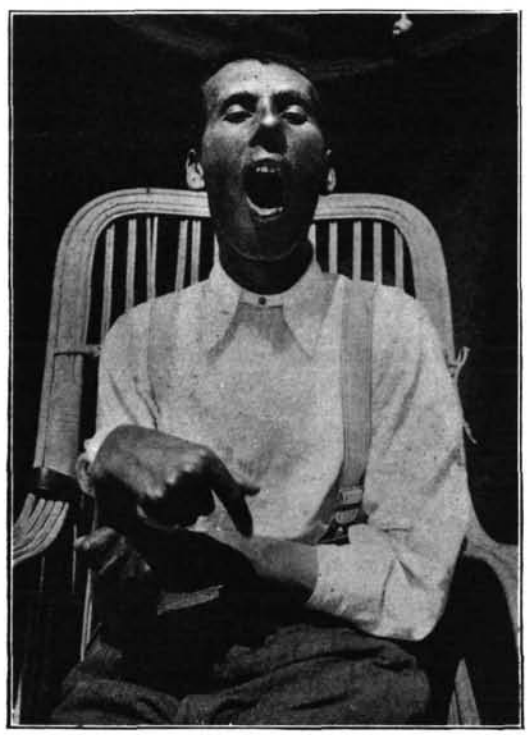

FIG. 21.—E. P. (June 4, 1910). Note vacant expression, open mouth, sialorrhœa, contractures. (Exposure $\frac{1}{15}$ sec., to counteract effect of constant tremor.)

No paralysis of the muscles supplied by the spinal accessory nerve was noted.

The tongue was thin and narrower from side to side in its middle section than nearer the tip. When he protruded it to command, there was much to-and-fro tremor as it moved slowly forward, but he managed to get it right out, and once it was well out the tremor ceased. Lateral movements were also performed, though very slowly. There was no fibrillary tremor, nor was it cracked or fissured.

MOTOR SYSTEM.

General muscular development was fair, but at the same time the musculature had obviously been shrinking and was in a state of poor nutrition. There was no local muscular atrophy to be observed anywhere, and no fibrillation.

Tone.—All the skeletal muscles, almost without exception, felt very firm to the touch, and this hypertonicity was probably one of the reasons for the slowness of the patient's voluntary movements. There was always a certain difficulty in impressing any passive movement on a limb, but it could be effected. If the arm was passively extended and flexed quickly at the elbow, insufficient relaxation impeded the movement; if it was done more slowly there was no difficulty. When any limb was placed in such a position as to relax the muscles as completely as possible it was found that they still felt firm. When the patient was voluntarily contracting, say, the left biceps, in the effort to flex at the elbow against resistance, the left triceps did not relax entirely, though it became for the moment less tonic.

The abdominal and the leg muscles were similarly rigid, palpation of the abdominal viscera for this reason not being easy.

The results of this generalized rigidity were rather curious. The patient seemed to be "soudé"—i.e., welded or soldered, after the picturesque French expression. He fell about *en bloc;* his back moved *en bloc;* sitting on the edge of his bed he would slowly lose his balance and fall over in a solid mass on to his side, often to his huge delight, at least in the presence of a visitor. The neck muscles were always in a highly tonic state; even when he lay with his head back on the pillow the sternomastoids did not relax. It was clear that the condition of the musculature had a great deal to do with the difficulty experienced by the patient in maintaining his equilibrium.

Speaking generally, the spasticity was more evident in the trunk and proximal sections of the limbs, whereas the tremor was most noticeable in the distal portions of the limbs, and affected the proximal joints and the trunk to a less extent.

It cannot be said that there was any specialized local myotonia. For although relaxation was slow, it was no slower than voluntary contraction; they were alike in this respect, nor was there any distinction between flexor and extensor groups, or between any muscular group and its antagonists, in the matter.

Contractures.—The hands and arms were, when left to themselves, held invariably in the position to be described (fig. 21). On the right side the forefinger was flexed at the metacarpophalangeal joint, but extended distally, and similarly with the thumb. These two fingers were in opposition, whereas the other three fingers were flexed at all the joints. The wrist was flexed to a right angle, the forearm semipronated and flexed on the upper arm, which was adducted at the shoulder. The whole position of the arm was suggestive of the attitude adopted by a hemiplegic limb with contracture, while there was a distinct resemblance to the attitude of paralysis agitans in the hand (fig. 22).

The left hand was curled up, with the thumb held inside the flexed first and second fingers; the wrist was not so much flexed as on the right side; the arm was flexed at the elbow and adducted at the shoulder.

The lower extremities were flexed at the knees, not to a great extent; the feet were somewhat inverted and the heels drawn a little up. The toes were slightly flexed.

As has been said, if the patient was left to himself, such were the apparent contractures of the limbs, and they never varied. But the interesting thing was that these were really "contracture-attitudes" which could be overcome, both actively and passively, to a very large extent, so that the degree of true permanent contracture could be estimated. It was found that the right arm

FIG. 22.—E. P. (June 4, 1910). Contracture-attitude of right hand. (Exposure $\frac{1}{250}$ sec., to obviate the effect of never-ceasing tremor.)

could not be completely extended at the elbow, nor could the legs be completely straightened at the knees. Apart from this the limbs could be passively moved in any way. Moreover, if the patient were given time, he could overcome these attitudes of contracture himself. He could open and close his right hand, flex and extend the fingers, abduct and adduct the same, &c.; in fact, he could make any movement at any joint, but slowly, not strongly, and always to the accompaniment of tremor. He could overcome the habitual position of the lower extremities in a similar way. In spite of the extraordinarily spastic appearance of the face, there was no true contracture of any of the facial muscles or muscles of the throat and neck.

Power.—All voluntary movements executed by the patient were certainly somewhat weak. There was no doubt of this. All could be resisted by the

examiner with comparative ease; the strongest relative movement seemed to be depression of the lower jaw.

In the arms the range of voluntary movement was unexpectedly good, considering the contractures of the limbs. The grasp was better on the left side than on the right; the left biceps was stronger than the right, whereas the right triceps was a little stronger than the left.

All voluntary movements of the legs were relatively better, but not of normal strength. On the whole the flexor groups were weaker than the extensor groups. Adduction at the hip was much stronger than abduction.

In any voluntary movement a jerky action was usually to be observed; when the patient voluntarily adducted his legs it was by a series of jerks, apart from the gross action-tremor which was constantly present. He seemed to be unable to sustain any movement for longer than a few seconds, although encouraged or urged to do so; relaxation began, and once the voluntary effort weakened the affected muscles passed into the ordinary unceasing tremor.

All the muscular groups of the body were tested as far as could be done, and, speaking generally, it may be said that the left side was weaker than the right, and not so tremulous as the right.

Tremor.—Undoubtedly the most striking motor phenomenon in the case was the highly typical rhythmical tremor of the arms and legs. As the patient sat in the sun a ceaseless to-and-fro, up-and-down movement of his extremities at once caught and riveted the attention. This tremor was a beautiful example of a true tremor—i.e., of a rhythmical alternation in contraction of a given muscular group and its antagonists. Its rate varied from four to six a second; it rarely quickened, perhaps, to eight a second. Its range or excursion was also variable; as a rule this did not exceed an inch in the case of the fingers, but with any muscular effort—e.g., in picking out the letters on his alphabet—the range was as much as 3 in. (about 7 cm.). On exertion the tremor became wide and quick; left to itself it was slower and finer.

In the arms the chief tremors were: alternating flexion and extension at the elbow, flexion and extension at the wrist, with the frequent addition of a slight alternating pronation and supination, causing a sort of rotatory tremor; the finger tremor was chiefly flexion and extension, sometimes with the addition of an opposition and adduction element in the case of the thumb. In the legs there was alternating flexion and extension at the knees, though this was of very short range; there was more obvious flexion and extension at the ankles, and most noticeable of all was the tremor of the toes. The lower jaw also, unless the mouth were at its maximum of opening, moved up and down rhythmically through a fine range. When the patient sat up on the edge of his bed there was a distinct to-and-fro movement of the body in an anteroposterior direction.

Speaking generally, the tremor was more noticeable distally than proximally, being in this respect the contrary of the spasticity, as has already been

remarked. When any muscular effort was made the tremor in the corresponding groups increased in degree and rapidity, and often spread; thus by making the patient squeeze my fingers in his hands I could augment the tremor of the lower extremities. With the finger-nose test the tremor was easily aggravated, but there was this difference in the two sides; on the left side the patient put the forefinger to the nose in the usual way, to the accompaniment of a tremor increasing in range, and in doing this the contracture of hand was relaxed, but the right hand in contracture-attitude was always put *en bloc* to the nose.

When it is said that the tremor increased with voluntary action it must be remembered that the patient was incapable of sustaining any voluntary effort for more than a few seconds, hence the increase in the rate and excursion of the tremor was always transient and of brief duration. When the finger or the hand reached the nose the tremor at once became less marked, although the limb was being held in the desired position.

A number of experiments were made to see if by supporting and relaxing all the joints of a limb the tremor would disappear. It was possible in this way, and by quietly encouraging the patient to divert his attention from what was being done, to cause the tremor to cease, *in toto*, for a few seconds. This was effected in the right arm, for instance. When it was left to itself, extended and still, without any interference on the patient's part, the limb almost immediately began to shake again, at first quietly, but with ever-increasing force, and at the same time it began to contract again at the joints, with the result that ere many seconds had elapsed it was back once more in the accustomed position, and shaking as before. The tremor which was the most difficult to cause to disappear was a fine interosseous tremor, coupled with the somewhat rolling tremor of the forefinger and thumb. The involuntary movements were never choreiform or athetoid.

Co-ordination.—No real inco-ordination was to be observed. Even when the tremor was severe, the patient could direct his forefinger to his nose correctly. The occasional irregularity of movement of the eyes could not be called ataxia. There was no static ataxia. When he stood upright, closure of the eyes made no difference to his equilibrium.

SENSORY SYSTEM.

The patient did not complain of any abnormal subjective sensations, and on examination no alteration in any form of cutaneous or deep sensibility could be detected.

REFLEXES.

A slight jaw-jerk was present. The tendon reflexes of the upper extremities were not easy to elicit, because of the tonic condition of the muscles. They were obtained, however, and were equal on the two sides. The abdominal reflexes were present, equal, active, and readily obtainable from all four quadrants. The knee-jerks and Achillis-jerks were brisk and equal; there was no ankle or other clonus. The plantar response was of unmistakeable double

flexor type. In regard to the organic reflexes, the patient was reaching the indifferent stage. His attendant put the bottle to him at regular intervals; if this was not done he passed urine "involuntarily." There was no doubt, however, that he could pass urine naturally; probably his helplessness was sufficient to account for the methods adopted. There was no incontinence of fæces.

GAIT.

This was a very interesting and instructive performance. As the patient was helped to his feet he leant hard on the supporting arm, moving stiffly and clumsily, and ready to fall in any direction, as the maintenance of balance was somewhat hazardous; at the same time there was a perfect riot of tremor. At first he was certainly rather on his toes, but in a short time the heels came down, and with shuffling steps, not unlike a *démarche à petits pas*, he proceeded, tending usually to fall forward. Nevertheless he improved with the effort, and was able to go up and down two steps, and walk along a corridor, slowly, laughing and shaking the whole of the time. He was totally unable to walk unaided.

Such, then, was the condition of the patient when I visited him in June, 1910. During the summer he remained much the same, but towards the autumn, without obvious reason, he began to fail rapidly. He became definitely worse about the beginning of September. Up to that time he had been getting up daily, and sitting as usual in the sun the greater part of the day. He developed an irregular temperature which ran up to nearly 104° F., suggesting possibly some kind of septic absorption. The difficulty of feeding the patient became acute. Slight sores appeared over the heels, trochanters, and sacrum. These were, however, more superficial abrasions than real bed-sores. The tremors of the limbs, especially of the arms, became more violent than ever, and the contractures much more marked. General emaciation rapidly set in. Yet the patient maintained complete consciousness to within a couple of hours of his death. He recognized all those around him, and knew quite well where he was. He was able as usual to express his wants by his alphabet. When asked if he wished anything to drink, he was able, though *in extremis*, to indicate his desires rationally. During these weeks he was incontinent of urine and fæces. He died on the afternoon of September 20, 1910, being then 22 years of age.

RÉSUMÉ OF THE CLINICAL HISTORY OF CASE 3.

A youth of 17, the brother of the patient whose case is No. 2, of normal mental and physical development, active and athletic, breaks down through overwork for an examination, suffers from auditory hallucinations, becomes excited and unmanageable, and is removed to Bethlem Hospital, where a diagnosis of toxic psychosis is made. This

illness is of comparatively brief duration, and the patient makes a complete recovery therefrom, never showing any analogous symptoms at any subsequent period. No signs of organic disease of the central nervous system are noted. In less than a year he is discharged recovered, and appears in good general health.

About four or five months later, the patient being 19 years old, other symptoms of a different nature make their appearance and progress rather rapidly. He begins to have difficulty in speaking and swallowing, and it is noticed that a little saliva escapes from the corners of his mouth. At the same time his hands become tremulous and his handwriting deteriorates. In the course of three months his whole appearance has altered for the worse. The tremor is generalized, his dysarthria is such that he rarely speaks at all; what he says is scarcely intelligible, and he has a constant tendency to keep his mouth wide open. The dysphagia also increases.

In the next year the disease runs a slow downward course. The patient's musculature becomes very stiff, so that his helplessness is considerable; his face wears a constant fixed smile; he is very cheerful, and often breaks into spasmodic laughter; the tremor of the limbs is severe and constant, and increases on exertion; the defect in articulation amounts almost to anarthria. Yet there is no obvious mental impairment beyond a certain childishness which shows itself in the readiness with which he is amused. He is able to read, understands everything that is said to him, indicates his wants, and evidently has a degree of intelligence of which a glance at his physical appearance gives little hint.

From this point the progression of the disease is even more noticeably in a downward direction. When he is just turned 22, about two and a half years from the onset of the illness, and three months before the end, an examination shows the following as the most noteworthy points:—

He has a fixed smile on his face, and bursts frequently into involuntary laughter; his mouth is wide open and the saliva dribbles from it; he cannot swallow, yet his palate moves well and he can protrude his tongue slowly, but completely; he cannot articulate, though he can phonate "ah" fairly well; he can perform upper facial movements well, lower facial movements very badly; there is no nystagmus, and the pupils react briskly to light. He is very thin; his muscles are all hypertonic, and he has an attitude of contracture, chiefly flexor, in the arms and legs; yet this contracture can be overcome passively, and also actively, although voluntary movements are very slow; there is no true

paralysis, yet the patient is very helpless, falling and rolling off his chair, owing to the muscular stiffness and weakness combined; his hands and arms, feet and legs, and to a less extent his trunk, show a ceaseless rhythmical tremor, which increases with exertion. The muscular hypertonicity is more marked proximally, the tremor distally. There is no disturbance of sensation. The abdominal reflexes are brisk and a double flexor response is obtained—accepted proofs of the integrity of the pyramidal tracts. With the help of an alphabet he is able to express his wants; he evidently appreciates all that is going on round him; his observation is quick, and he understands everything that is said to him.

Three months later he becomes more acutely ill, his temperature rises, he becomes much weaker, emaciation rapidly progresses, bed-sores and more permanent contractures develop, and, conscious to within an hour or two of the end, he dies, at the age of 22, after an illness of three years' duration.

At no time during his illness, or before, has he shown any of the ordinary symptoms or signs of cirrhosis of the liver.

Case 4.—M. To., aged 20, was admitted to the National Hospital, under the care of Dr. Tooth, on October 20, 1911. She was born on September 19, 1891, and was the third child and only daughter of the following family:—

(1) Male, died, aged 10, of what is said to have been tuberculous peritonitis.
(2) Male, aged 22, alive and well.
(3) Patient (Case 4).
(4) Miscarriage.

Family history.—Both parents at the time of writing are alive and well. On the paternal side there was a history of "liver" complaints among various members of the family, usually in the form of "headache, sickness, or indigestion." The grandmother on the father's side suffered from jaundice once or twice, but lived to the age of 78. The patient's father had "suffered from his liver" all his life in the shape of "bilious attacks." When he was born his mother was suffering from an attack of jaundice. On the maternal side there was a tendency to "weak chests" among several members of the family.

Previous history.—The patient was never very strong, but, on the other hand, had had no serious illness at any time. About five years before coming under observation she had a moderately acute attack of jaundice, which lasted rather more than three weeks. No ill-effects followed this illness apparently, nor did the icterus return. From that time the patient had never shown any symptoms referable to disturbance of the liver. Menstruation was established at the usual age, and was regular up to the commencement of the present illness more than a year ago, since when the patient had menstruated only

twice, on each occasion losing a large quantity. Since the age of 18 she had become very tall.

History of present illness.—About the month of May, 1910—i.e., about one and a half years before the patient entered hospital—it was remarked that her handwriting was not quite so good as it had hitherto been, and that there was an almost imperceptible tremulousness of the right hand. A few months later this tremor of the hand became definitely noticeable in the performance of fine movements, such as needlework, and about the same time the right lower extremity was also occasionally seized with slight tremulousness. From its onset the tremor of the right limbs steadily progressed. It was at first considered that the condition was functional, and a Weir-Mitchell rest cure of some weeks was carried out, but without much result. In addition to the tremor the patient presented certain indications of pulmonary weakness, but although this condition responded well to treatment and eventually disappeared, the nervous symptoms remained. About a year ago her parents noticed that the patient's voice was becoming a little husky, and her articulation a little indistinct. About six months before her admission to hospital definite dysarthria and dysphagia made their appearance, and these symptoms, too, progressed without remission. The patient used to be fond of going long walks, but since that time her legs became weak and stiff; she could only take short walks, and tired readily. In the course of a month or two she found herself unable to walk without strong support. Within the last three months the left hand and arm started to tremble, but not so constantly or so severely as on the right. It was frequently remarked that with any attempt at voluntary movement of the right limbs they were thrown into tremors, and observing this herself, the patient took to shaking hands with her left hand instead.

During the last six months the difficulty in swallowing and in mastication had been such that the patient could not bite satisfactorily, and was unable to swallow anything but fluids, or bread and butter. The latter was pushed to the back of the throat before she could swallow it. The dysarthria gradually degenerated into complete anarthria. The end syllables of words were slurred over, until her speech became unintelligible. Occasionally, in the mornings, the patient was still able to articulate a few words more or less clearly. It was noticed that sometimes the patient's lips and tongue moved as though to form a word, but no phonation was accomplished.

During the three months prior to her admission to the National Hospital, the symptoms above enumerated all increased in severity. In addition, contractures of the limbs appeared, more particularly on the right side. The limbs became stiffer and more difficult to move, till at length the patient could not completely extend her right wrist or fingers. With this rigid condition of the muscles they began also to waste, no doubt in part as a sequel to inadequate nutrition, and when the patient came under notice she was very thin indeed. There was, however, no special wasting of any particular muscle or group of muscles, if exception be made of the fact that the right shoulder muscles were perhaps thinner than on the left side. Her face was

expressionless and fixed in a mask-like tonic contraction, the mouth being constantly held open, while saliva slowly dribbled from the corners. Any effort at articulation resulted in the appearance of tremors in the neck and trunk, especially if the effort was sustained. There was often a fixed smile on the patient's face, but exaggerated emotionalism was not conspicuous, nor was there a true "rire spasmodique." Her mental condition throughout appeared to be quite satisfactory. She read novels with avidity; took an intelligent interest in topical events; was correctly oriented in time and space, and suffered from no abnormal condition such as delusions or hallucinations.

During the last few weeks there had been some difficulty in passing water, which was relieved by the application of hot fomentations. There had been, also, a good deal of constipation.

Condition on admission.—The patient was a very tall and thin young woman. Her height was about 6 ft. 2in., but she did not weigh more than 8 st. There was no sign, subjective or objective, of pulmonary mischief. The urine, of specific gravity 1015, contained a few pus-cells microscopically.

She looked bright and intelligent, in spite of the vacant facies; with her eyes she followed the events of the ward with quickness and alertness, and it was clear she was fully cognizant of all that was done for her and of the details of the examinations to which she was subjected. All questions were answered to the best of her ability, by gesture or otherwise, and all requests were obeyed with readiness. In the appreciation of written and spoken language there was no defect whatever. No explosive laughter was noticed, yet the patient was probably a little more emotional than normal. The contrast between the opened, fixed mouth, with saliva dribbling over the chin, and the peculiarly lively expression of the eyes, was remarked by all who observed her.

When the patient laughed some sound came from the throat, otherwise phonation was practically absent. It was odd to note the emission of this scarcely recognizable sound from an immobile face. Articulation was also almost absent. She could make sounds approximating to "yes" and "no" in a whisper, also certain other words which those who knew her best were occasionally able to determine.

She complained of nothing in particular; was not in pain; and at the same time gave no definite indication of mental distress at being unable to express herself.

CRANIAL NERVES.

Visual fields, vision, and optic discs were all normal.

The pupils were equal, regular, of medium size, and of normal reaction in every way. The ocular movements were normal. There was no nystagmus in any direction.

The mouth could be opened to its full extent, but the patient was unable to bring the teeth firmly together. Lateral movements of the inferior maxilla were very imperfect. Biting and chewing were impossible.

There was no defect of facial sensibility. The corneal reflex was brisk on both sides.

The more or less constant facial expression of the patient is seen in fig. 23. The upper teeth and a good part of the upper gums were always visible; the corners of the mouth were retracted in a stiff and rather fatuous smile; with the exception of slight play of the eyelids, expressing pleasure or otherwise, the facial musculature was rigid and immobile. She could not whistle, but could slowly purse up her lips to form a more or less circular opening. The eyes could be opened and shut with some power.

FIG. 23.—M. To. (National Hospital, October, 1911). Characteristic fixed smile and retracted lips. Note intelligent expression of eyes. The patient is falling stiffly to the right.

Hearing was normal on both sides.

The dysphagia and anarthria have already been referred to. In spite of the anarthric condition the patient's soft palate rose fairly well and symmetrically on the effort to phonate. The palatal reflex was brisk from either side.

The sternomastoids were in a state of hypertonicity, and did not relax though the patient was reclining. The head could be rotated slowly from side to side, to the accompaniment of tremor of the head and trunk.

The tongue, though rather thin, was not atrophic, and showed no sign of fibrillation, nor was it puckered or fissured. It could be protruded slowly,

and in a straight line, but only for a short distance. Lateral movements of the tongue were not so good.

MOTOR SYSTEM.

The musculature throughout was very thin, the wasting being generalized. No fibrillation was detected. The case presented the characteristic motor symptoms of tremor, rigidity, and contracture, and these may be described in turn.

(*a*) *Involuntary movements.*—The right arm and leg were in a state of continuous clonic tremor—a regular rhythmical involuntary movement affecting all the joints of the limbs, and not, in this case, more marked distally than proximally. The excursion was wide and the rate rather quick, about three or four a second. During the waking hours it was never absent. With excitement or exertion it sometimes became violent, the right leg and foot striking the bed in a rapid succession of rhythmical alternating flexion and extension movements, mainly from hip and knee. Unless the right arm were held by the side its tremor became coarse and severe. A similar tremor was present in the left limbs, but here, while of the same regular and alternating type, it was certainly less pronounced and sometimes scarcely to be detected. Further, voluntary control over the tremor of the left half of the body was less impaired than over the right. With strong muscular effort against resistance the tremor always exhibited a tendency to become generalized in head or trunk, or to spread to the lower extremity when the upper was prevented from carrying out a given movement. There was less tremor of the interosseous and small-hand muscle type in this case than in the others which I have observed, but occasionally such involuntary movement could be seen. The movements of the limbs were never choreiform or athetoid.

(*b*) *Rigidity.*—The right arm and leg, and to a less extent the left, were in a state of hypertonicity, which, as far as the former are concerned, could only be described as extreme. Fig. 24 gives some idea of the general attitude of the upper extremities. The right arm was flexed at all joints, with the exception of the terminal joints of the fingers. So great was the flexion at the wrist that the fingers almost touched the middle of the forearm. The right leg was in extensor spasm, the foot being in a somewhat equinus position, and the right great toe slightly dorsiflexed. On the left side the arm and leg were in more or less analogous positions, but the spasticity was not quite so great, although evident enough. Everywhere the musculature was firm and hypertonic. Of this one could easily convince oneself not merely by palpation but by impressing passive movements on the various segments of the limbs, when it at once became obvious that whether the movement were one of extension or of flexion the antagonists were in each case equally resistant to the movement. As the patient lay in bed the generalized spasticity of the musculature gave the patient the appearance of being, as it were, "soldered," an impression the effect of which was heightened by the slowness of her voluntary movements. When she stood upright, her feet together, she always tended to fall "like a

pillar," indifferently in any direction. The abdominal muscles were peculiarly tense and firm, and never relaxed. The trunk moved *en bloc* when the patient endeavoured, on request, to bend her body forwards or backwards.

(*c*) *Contracture.*—Definite contracture had set in at various joints—a true contracture, which could not be overcome by passive movement. It was impossible to raise the right arm beyond a right angle at the shoulder; at the elbow the arm could not be quite completely extended. The forearm could not be put into a position of full supination. The flexion at the

FIG. 24.—M. To. Note characteristic contracture-attitudes, tremor of right hand (the patient is grasping her nightdress with that hand in the endeavour to keep the limb as steady as possible), open mouth, vacant expression.

wrist could only be undone to a slight extent. The skin on the anterior aspect of the right wrist was raw as a result of the continued flexion. The right leg could be bent up fairly easily; passive flexion and extension at the various joints were not materially interfered with. On the left side the condition was one of "contracture attitude," without true contracture. Thus at all joints passive movements were possible, and could be carried out completely, although the limbs appeared to be in as extreme contracture as those of the opposite side.

(*d*) *Voluntary movement.*—There was no doubt that voluntary movements were weak, apart from the spasticity and contracture. The patient could extend the right arm at the elbow to about a right angle, but not further. When the right fingers were passively unbent she was able to grasp fairly well. She was unable voluntarily to overcome the contracture at the right wrist. Voluntary movements of the right leg could be effected at all joints, but they were weak and slow. Similarly the left arm and leg could be used voluntarily at all joints, but again in a slow and stiff fashion. There was no paralysis in the real sense of the word, for the patient could innervate and actuate voluntarily all her muscular groups; where no movement occurred the displacement of the segment concerned was prevented by contracture, not by paralysis.

No inco-ordination or ataxia was discoverable.

The patient could walk slowly and stiffly, but quite steadily. She stood upright without swaying if the feet were a little apart. Closure of the eyes caused no unsteadiness.

SENSORY SYSTEM.

No change in sensibility was present. All the usual tests for sensation were utilized in the examination.

REFLEXES.

The arm-jerks were brisk, a little more so on the right than on the left.

The abdominal reflexes could not be obtained owing to the great rigidity of the abdominal muscles. The knee-jerks were present and equal, not exaggerated. The ankle-jerks were present and equal. There was no clonus. The left plantar response was flexor; the right, more difficult to obtain, appeared to be flexor. The function of the organic sphincters was normal.

The only other point to be mentioned in the examination is that there were no indications of liver disease; there was no œdema, no ascites, icterus, or distended veins. The liver reached from the fourth intercostal space to 1 in. (2.5 cm.) above the costal margin—i.e., 5 in. (about 12 cm.) in the right mammillary line.

RÉSUMÉ OF THE CLINICAL HISTORY OF CASE 4.

A girl, aged 18, who had an attack of jaundice some four or five years previously, but whose mental and physical development has been up to the normal standard, is noticed to develop a certain tremulousness of the right hand, so that her writing deteriorates, and she is somewhat awkward in the performance of fine movements with the fingers. A few months later the right leg begins to show some shakiness, and at the same time articulation becomes a little defective. So slight are the signs, however, that a rest cure is undertaken in the hope that the condition will thus clear up. But the symptoms steadily progress,

and definite involvement of the nervous system can no longer be denied. The limbs very gradually become stiff, more especially on the right side, and walking becomes more difficult; certain contractures appear in the right arm. As a result of an increasing dysphagia, which is associated with the dysarthria, the patient gradually emaciates, though there does not appear to be any local wasting of muscles. Within a year and a half of the onset of the disease she has become completely anarthric; her muscles have become extremely hypertonic both in trunk and limbs, yet her voluntary control over them is very fair; the upper extremities are fixed by contracture in the attitude of flexion, there being a true contracture on the right side, but only a "*contracture-attitude*" on the other, for the patient is still able to move that limb at all the joints. Along with the hypertonicity and contracture there is a never-ceasing rhythmical tremor of the limbs, sometimes also of head and trunk, coarse in type, and sometimes violent, which is more noticeable on the right side.

Examination shows that the pupil-reflexes are normal; the optic discs are normal; there is no nystagmus; there are no sensory changes; there is no clonus at the ankle, and a flexor plantar response is obtained on the left side, and with some difficulty, owing to contracture, on the right. There is no sphincter impairment. It may be said, therefore, that the so-called "signs of organic disease" of the pyramidal system are awanting, but the anarthria, dysphagia, tremors, spasticity, and contractures present a clinical picture indicative of a profound disturbance of motility. The face is immobile; the corners of the mouth are retracted in a spastic smile; saliva runs from the lips; the mouth is widely open; only the lively and interested expression of the eyes remains to show that the patient's mental condition is one of alertness and intelligence. There are no indications at all of hepatic disease.

Case 5.—Samuel M., the eldest member of the M. family, was born in 1864, and was quite well as a child. He developed in a normal manner, physically and mentally, and was in good health till the age of 9. At this age he accidentally fell into the Regent's Canal, and soon after developed typhoid fever. It was a severe attack, lasting, with relapses, over the better part of six months.

Rather less than a year later, when he was 10 years old, it was noticed that his fingers and hands were beginning to shake when he used them in any muscular effort, and that he could not walk properly. His gait began to be somewhat shaky. The condition gradually got worse. About a year or so from the commencement of the illness he began to suffer from an articulatory defect and swallowing became difficult. In the course of another year the

extremities became contracted, and he had to be fed and nursed by others owing to his helplessness. He used to keep his mouth open and to "make a groaning noise." He was admitted to the National Hospital some time in the year 1878, but the notes cannot be found. He was discharged unimproved and taken home, where his condition steadily deteriorated. He was "reduced to skin and bone," and so helpless that "he could not move hand or foot." Anarthric, dysphagic, emaciated and contractured, he lay in bed with all his limbs "constantly on the work." He died in 1879, aged 15 years all but a few days, after an illness of about four and a half years' duration.

Case 6.—Christopher J., aged 13, was admitted to the National Hospital, Queen Square, under the care of Dr. Thomas Buzzard, on January 18, 1889, with the following history :—

Two years before, for no obvious reason, the boy began to have difficulty in walking; he dragged his feet along the ground instead of lifting them properly, and his feet began to turn in slightly. About the same time he had to leave the choir in which he sang owing to "loss of voice." It was not that his voice broke, but he could not phonate properly.

A few months after the commencement of the illness some discoloration of the lower extremities was noticed. Bright purpuric spots appeared on the skin and faded gradually. At intervals since that time, crops of these spots appeared. There was no fever, but the joints were sometimes slightly swollen. Since then, the patient gradually became weaker on his legs.

About thirteen weeks before his admission he had œdema of the legs and scrotum, and some ascites. These symptoms improved. About a month before admission he had some difficulty in controlling the action of his sphincters. Formerly he was a bright and intelligent boy, in the sixth standard, but since the illness commenced he became duller and more stupid, noticeably so during the last month.

The patient was an only child; the parents were perfectly healthy, and the mother had had no miscarriages.

On admission he was seen to be pale and rather delicate-looking. His mental condition was striking; he was very emotional, at one time laughing, at another crying. He was slow in answering questions, and the saliva often dribbled from his open mouth. He was slow in understanding what was said to him, but did everything correctly that he was asked to do. There was some general wasting of the musculature, most evident below the knees, and there was some contracture at the ankle, as the patient was unable to move that joint, or only to a very little extent. The toes were in a state of more or less constant rhythmical tremor. Passive movements at the ankle were not easy of execution, and caused the patient pain, though not of any severity. He could move the legs well, but less well distally than proximally. The deep reflexes in the legs were increased, and there was a tendency to ankle-clonus on both sides. The plantars were "brisk."

In the arms all movements could be carried out, but were undoubtedly weaker than normal. The arm reflexes were active and equal. The abdominal

and epigastric reflexes also were brisk, and equal on the two sides. The pupils, optic discs, and ocular movements, were all normal.

The illness progressed rapidly; the boy's emotional state became aggravated; he laughed or cried on the slightest provocation. His legs became more contracted, and were constantly drawn up at the knees and hips. Constant sudden involuntary movements of the lower extremities occurred; they were abruptly drawn up and rather more slowly relaxed. The arms in their turn became rigid; the left arm began to contract up, and there were sudden involuntary alternating movements of pronation and supination to be observed. The same thing was noticed in the right arm, to a less extent.

Œdema and ascites set in and on February 14 the child died.

If we summarize this case briefly, its salient features are as follows:—

A little boy, aged 13, who has always been healthy and intelligent, begins to have difficulty in walking, and his voice alters; he becomes gradually more emotional, laughing or crying at the merest trifle; his mouth is open and saliva dribbles away; his muscles waste and become rigid, and then the extremities contract, the legs first, and later the arms; there is rhythmical tremor of the feet and toes, and attacks of involuntary spasmodic movements in the upper extremities, usually of an alternating type (pronation and supination, flexion and extension); he loses control over his sphincters. The abdominal reflexes remain brisk, however—a significant fact. Emaciation sets in, and he dies after an illness of about two years' duration.

He has shown very definite signs at intervals of defect of liver function, but there is no evidence of congenital syphilis.

Chapter III.—Pathological Findings in the Personal Cases.

In this chapter is given the complete pathological examination of three personal cases of progressive lenticular degeneration whose clinical history has been recorded in the previous chapter. In addition, there is a brief account of the pathological findings in Case 6, that is to say, the case referred to by Ormerod in his paper, the details of which have not hitherto been published. In Case 5 there was no pathological examination.

The harmony in the pathological findings of the personally observed cases is no less convincing than the similarity in their clinical features. It is true that the pathological investigation of Case 2 is not as complete as I should have liked, but there is ample evidence that its place with the others is beyond cavil. Cases 1 and 3 are identical,

pathologically, except that the latter is not so advanced as the former. It is, in fact, a fortunate circumstance that the degree of pathological change is not so great in Case 3, for clinically the patient was almost as profoundly affected as the patient whose case is No. 1. By this means what pathological change to associate with the clinical symptoms can be more readily determined, and due reference will be made to this important point in a subsequent chapter.

There are certain features of the pathology of the three personal cases which may very briefly be emphasized by way of introduction. In the first place, there is no pathological evidence that the cases are syphilitic; in fact, syphilis may be excluded pathologically, as I believe it can be clinically. The two earlier cases were under observation in pre-Wassermann days, while in the third case I had no opportunity of applying the test. Secondly, there is no pathological evidence that the disease is congenital, nor are there anomalies of development of any kind. Thirdly, the pathology furnishes proof that a selective morbid agent of a peculiar and perhaps unique kind must have been at work.

Case 1.—The autopsy was performed by myself at 9 p.m. on the evening of Wednesday, July 29, 1908, twenty-five hours after the death of the patient, in hot weather. The body was greatly emaciated, and rigidity was profound, but there were no bed-sores or abrasions. *Post-mortem* lividity was pronounced.

On opening the calvarium the dura was neither adherent nor discoloured; its veins and sinuses were engorged, but otherwise normal. The subarachnoid spaces and cisterns were greatly distended with cerebrospinal fluid. The arachnoid was observed to be somewhat "milky" at the base of the brain, in particular across the interpeduncular space. The arteries at the base presented no visible abnormality. The pons, cerebellum, medulla and cord seemed normal on a rapid inspection. The membranes of the cord were not thickened. As the cranial nerves were cut through they appeared to be normal.

The brain and cord were immersed in 10 per cent. formalin. They were weighed the next day, with the following result: Brain complete, 1,350 grm.; cerebellum, medulla, and pons, together, 146 grm.; cerebrum, 1,204 grm.

The heart and lungs were normal, except that the latter were somewhat congested. There were old pleural adhesions, few in number, on the left side posteriorly.

The liver, when removed from the abdomen, presented a very striking appearance, seen in figs. 25 and 26. It was intensely cirrhotic; the whole of its surface was covered with irregular rounded nodules of liver-tissue, about the size of small hazel-nuts, surrounded by bands of connective tissue, of

FIG. 25.—Liver (S. T., Case 1), from above.

FIG. 26.—Liver (S. T., Case 1). Transverse section.

varying width. Some nodules were considerably smaller. The capsule of the liver was not obviously thickened, except in one or two places. There were no adhesions to the neighbouring viscera. The organ was not bile-stained, and was perhaps rather lighter in colour than usual. On making a transverse incision through it, it was seen to be cirrhosed from one side to the other; it was divided up into nodules varying in size from a shilling to a threepenny-piece, or less, between which was a great deal of connective tissue overgrowth, sometimes of considerable width, especially in the deeper parts of the viscus. There was much thickening along the portal tracts. The cirrhosis was mainly multilobular.

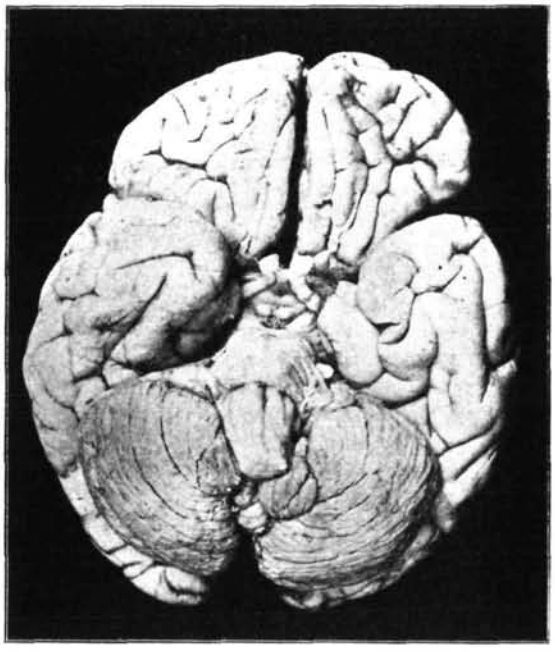

FIG. 27.—Basal surface of brain (S. T., Case 1).

The weight of the liver and gall-bladder was 1,380 grm. It was very firm and preserved its shape. The gall-bladder did not show any abnormality.

The spleen was not obviously enlarged; it was firm and rather congested, and its cut surface on section seemed normal.

The kidneys were normal.

The pancreas and the intestines were unaltered. The stomach was three-parts full of dark liquid blood; its mucosa was greatly congested, but no ulceration was discovered, and a rapid search for a ruptured vessel or vessels was unsuccessful.

There was no ascites.

The suprarenal on the left side, pieces of the following muscles—right thenar eminence, left biceps, left flexor sublimis digitorum, left extensor communis—together with a piece of the left lobe of the thyroid, were taken for subsequent examination.

Macroscopical Examination of the Brain and Cord.

After hardening in formalin the brain was stripped of its membranes. These were not adherent anywhere. Pieces of the middle cerebral artery and its branches were taken for microscopical investigation.

The cerebral hemispheres were well developed and did not show any atrophy or undue spacing between the convolutions. The pattern of the latter was normal (figs. 27 and 28). In particular the frontal lobes were not the

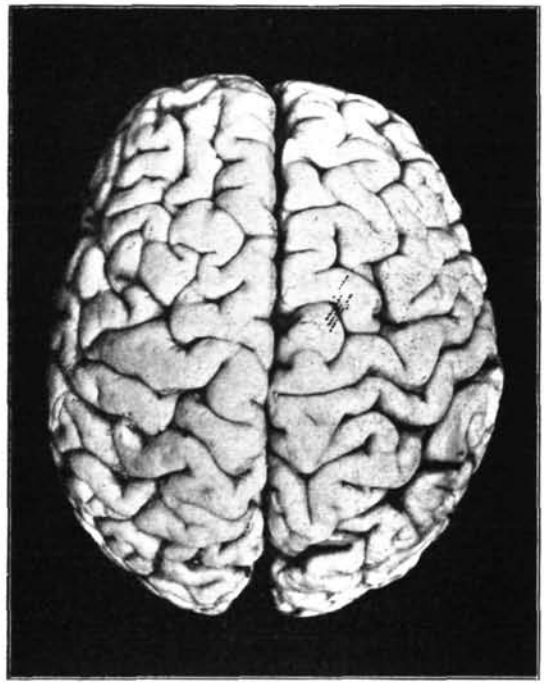

Fig. 28.—Upper surface of brain (S. T., Case 1).

seat of any obvious naked-eye pathological change. The corpus callosum was divided in the mesial plane, when the mesial aspect of the hemispheres was examined and found to be normal.

Each hemisphere was then cut across by Pierre Marie's *coupe d'élection*, a section which passes under and just touches the extremities, anterior and posterior, of the corpus callosum as it appears on the mesial aspect, and is

carried horizontally outwards to the lateral aspect of the hemisphere. When this was done the picture reproduced in fig. 29 was revealed.

The eye was at once caught by a remarkable bilateral and symmetrical cavitation of the lenticular nucleus; its severity in degree seemed the more

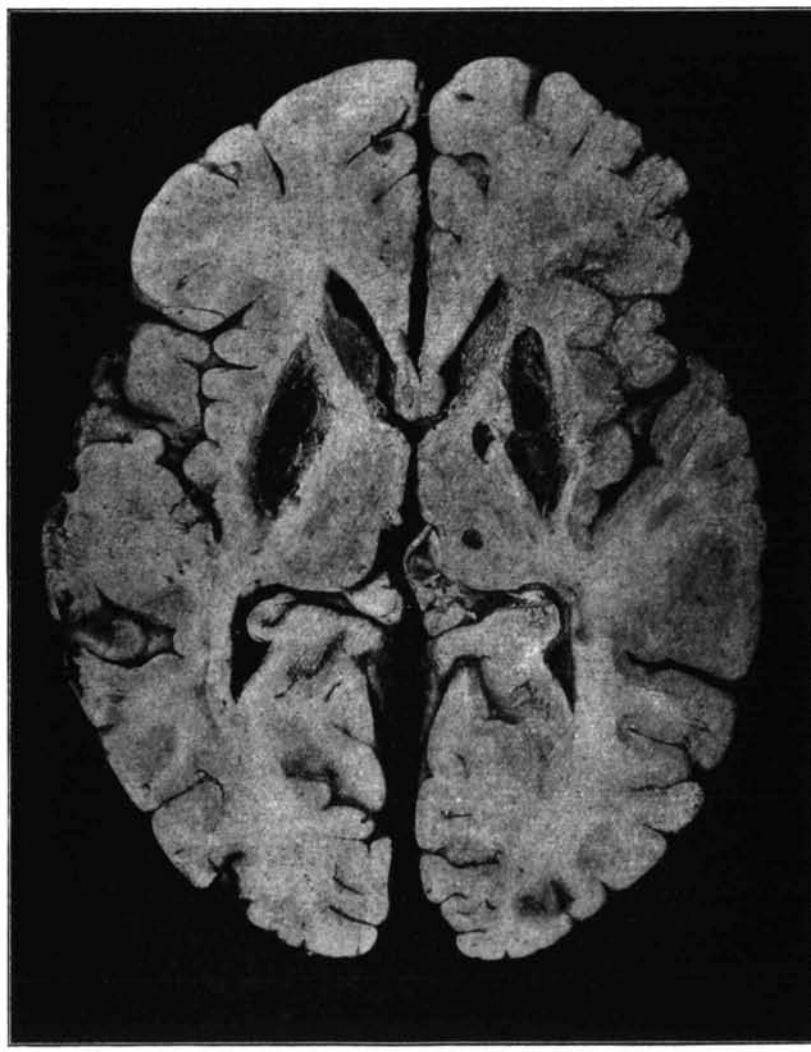

FIG. 29.—Horizontal section through hemispheres (S. T., Case 1). (They are reversed in the figure, the left being at the right-hand side.)

astonishing since the rest of the cut surface of the hemisphere was normal. The cortex and the white matter of the hemispheres did not present any abnormality; the thalami were of good size and shape; the internal capsules stood

out clearly (with an exception, to be noted immediately), but the putamen and globus pallidus had almost entirely disappeared, and in their place on each side was a crumbling cavity.

Right side.—Almost the whole of the right putamen, with the exception of its anterior fifth, and the globus pallidus, with the exception of its extreme inner part, were destroyed, while the small sections that remained were soft and disintegrated. In their place was a cavity lined with irregular dirty brown tissue débris, which subsequent examination showed to extend from the upper to the lower limit of the lenticular nucleus. Its greatest dimensions were $2\frac{1}{2}$ cm. long by $1\frac{1}{4}$ to $1\frac{1}{2}$ cm. wide. It did not contain any fluid. The outer margin of the cavity was formed by a steep wall which corresponded strictly to the outer aspect of the nucleus, and was sharply differentiated from the claustrum and island of Reil convolutions, which, although subsequent microscopical examination showed they were slightly degenerated, certainly did not present any sign of loss of substance. Posteriorly the cavity came to an end at a point corresponding to the posterior end of the nucleus, while its inner wall was formed by the internal capsule, except at the anterior part, where a little piece of globus pallidus tissue remained.

The external capsule in its middle third was thinned and had undergone loss of fibres. The caudate nucleus was somewhat shrunken, but compared with the destruction of the lenticular nucleus it was well preserved, and its fine fibres could be easily distinguished.

The internal capsule was untouched, though it looked rather undermined in one place; its anterior and posterior limbs looked perfectly normal. A few fine internuncial fibres from the extreme anterior part of the putamen, running mesialwards, could still be seen. The optic thalamus was to all appearance normal. The rest of the section presented no visible morbid appearance.

Left side.—The cavity formation on the left side was almost identical with that on the right. It was, however, even more severe. It occupied the whole of the lenticular nucleus, with the exception of a small portion of the globus pallidus anteriorly and to the inner side. It extended right back to the point at which the nucleus came to an end. On the outer side the cavity had destroyed part of the external capsule, at the junction of its middle and posterior thirds, and had extended into the claustrum slightly. Anteriorly, on this outer side, the crumbling débris of the nucleus had fallen away from the "bed" in which the nucleus lay, leaving a clean-cut edge to the cavity which is well brought out in the figure. On the inner side the cavity had undermined the internal capsule at its genu, and a small extension from the main part had made its way across the capsule, separating but not destroying the fibres, at least not to any extent, as will be seen later.

The cavity walls were highly irregular, and dark brown in colour; the débris that was left was soft and granular. Subsequent investigation showed that on this side also the cavity occupied almost the whole extent of the lenticular nucleus in a vertical direction. In one or two places thin strands of shreddy material still bridged it across, more particularly towards its

anterior end. Its dimensions were $2\frac{3}{4}$ cm. long by $1\frac{1}{4}$ cm. broad. The diameter of the little prolongation of the main cavity across the internal capsule was 7 mm. There was no brownish slough in this little subsidiary cavity, and no sign of softening round it.

The anterior limb of the internal capsule was normal. At the genu was the cavity prolongation already described. The posterior limb of the internal capsule looked quite normal, though it appeared somewhat undermined by the cavity; the retrolenticular segment was normal.

As on the right side, the caudate nucleus seemed rather small, and less rounded than usual, but it was not softened; in fact, it appeared well preserved and its internuncial fibres stood out prominently. The latter had all disappeared from what was left of the globus pallidus on this side.

The optic thalamus contained towards its posterior and inner side a small shallow, almost circular, depression, like a little punched-out hole, which was sharply defined, had no softening round it, and was not connected with the main cavity. Its diameter was 3 mm. Otherwise this ganglion was normal to all appearance; it was not atrophic or shrunken in any way.

The convolutions of the island of Reil did not show any obvious loss of substance.

The rest of the section presented no visible morbid appearance.

There was no internal hydrocephalus, and no ependymitis. The whole of the visible cortex on these sections appeared of good depth.

The spinal cord seemed, on naked-eye investigation, to be of normal appearance. Its transverse sections, at various levels, were of good size, and did not show any trace of degeneration. The membranes were not obviously thickened, unless it were that the pia-arachnoid was a little "milky," chiefly along the posterior aspect of the cord.

Microscopical Examination of the Nervous System.

(1) *Muscles.*—Sections were stained by the following methods: Hæmatoxylin-eosin, hæmatoxylin-Van Gieson, Weigert-Pal for intramuscular nerves, counterstained with eosin.

Speaking generally, the muscle-fibres were all of good size, and all about the same size; there was no disparity in this respect. There were no hyaline changes, no splitting of fibres, no loss of longitudinal or cross striation. What was chiefly remarked was a frequent change in the contour of the fibres, whereby they became more rounded, and less polygonal or polyangular than usual. In addition to this change, the muscle-fibres were often less closely packed together, and a degree of commencing interstitial change was frequently observed.

In some places the sarcolemmal nuclei were much increased in numbers. The muscle-spindles were normal, and no change was discovered in the intramuscular nerves.

(2) *Peripheral nerves.*—These were not separately examined.

(3) *Spinal cord.*—The histological methods utilized were: Weigert, Weigert-Pal, Nissl, hæmatoxylin-eosin, hæmatoxylin-Van Gieson.

(*a*) *Fibres.*—A glance at figs. 30 to 32, from sections stained by Weigert's original method, will show that there was no systematized degeneration in the cord. The white matter everywhere stained well. The pyramidal tracts were normal throughout, and stained deeply and equally. There was no shrinkage of the white columns, although there was a trace of marginal loss of fibres.

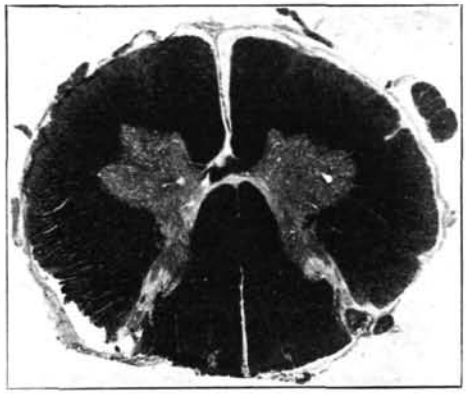

FIG 30.—Cervical cord (Case 1). Weigert.

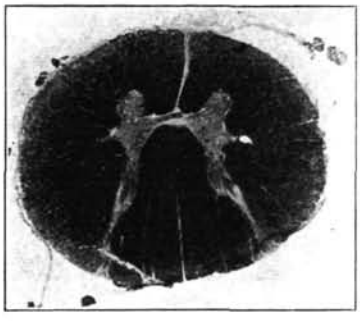

FIG. 31.—Dorsal cord (Case 1). Weigert.

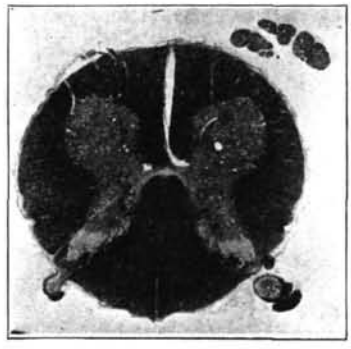

FIG. 32.—Lumbar cord (Case 1). Weigert.

The fibres of the grey matter also stained well, and were not apparently reduced in number. The integrity of the pyramidal paths in the cord is a significant fact in view of the complete motor helplessness of the patient, and of the contractures, tremors and hypertonicity.

(*b*) *Cells.*—These were carefully examined at various levels (fig. 33). In the first place they were present in good number, and preserved their normal

grouping. The majority, in both cervical and lumbar enlargements, were of good shape and staining reaction. A number, however, were rather elongated, and stained more deeply than usual, apparently owing to some shrinkage of the achromatic part of the cytoplasm, whereby the tigroid elements were brought more closely together, thus rendering the hue of the cell darker. Such cells retained their nucleus, and there is no reason to suppose that they had lost their function completely. Cells of this type are often met with in chronic diseases of the nervous system, in which the patient has not the full functional use of his limbs. Other cells, much fewer in number, showed commencing

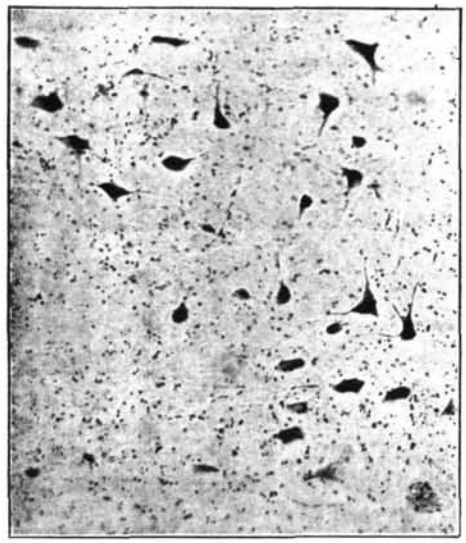

FIG. 33.—Anterior horn-cells, cervical region (Case 1). Nissl.

pigmentary degeneration. Others showed the changes that are associated with a more acute degenerative process—viz., pulverization of the chromatin elements round the nucleus, excentricity of the latter, and disappearance of its membrane. Such cells usually appeared somewhat swollen. In this case their presence may be indicative of a terminal infection.

On the whole, the actual numbers of the anterior horn-cells were apparently slightly reduced compared with a healthy—i.e., normal—cord.

(*c*) *Meninges.*—There was slight pial thickening round the cord, more especially in the cervical region. It is important to note, however, that small-cell infiltration was entirely absent. Neither in the meninges nor round the spinal vessels was there any trace of inflammatory reaction. The spinal vessels themselves were normal; they were not thickened in any of their coats, nor could anything approaching endarteritis be discovered. The intramedullary vessels similarly were healthy.

(4) *Medulla oblongata and pons.*—The same methods were utilized for these as for the examination of the cord.

With the Weigert-Pal stain for medullated fibres no change could be detected (fig. 34). The pyramids stained normally, and were not apparently

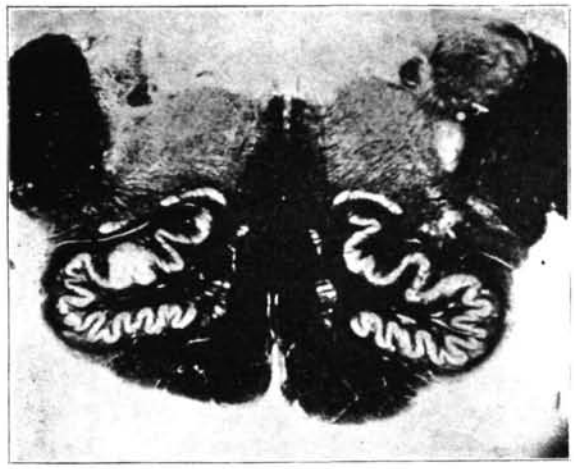

FIG. 34.—Medulla (Case 1). Weigert-Pal.

FIG. 35.—Hypoglossal nucleus, right side (Case 1). Nissl.

atrophic; they did not appear to have undergone any gross loss of fibres. In the position of the descending mesencephalo-spinal tracts no defect could be found. The olives, restiform bodies, fillet, &c., were to all appearances normal.

The cells of the motor cranial nuclei were investigated by Nissl's method. Fig. 35 shows the appearance of the cells of the right hypoglossal nucleus. It will be seen that there was no obvious loss of cells, distinguishing the condition at once from an ordinary bulbar palsy. Many revealed that alteration which has already been noted in some of the cells of the anterior horns—i.e., they were drawn out, stained more deeply, and were less easy to differentiate structurally, but retained their nucleus. The processes of the cells were elongated and often rather more wavy than usual. Examination of the nucleus shows that the "uselessness" of the tongue during life was not due to any atrophic paralysis.

The cells of the other motor cranial nerve nuclei examined were found to be similar to those just described.

FIG. 36.—Crus cerebri (Case 1). Weigert-Pal.

(5) *Cerebellum.*—From the structural point of view, as regards both cells and fibres, this organ was normal.

(6) *Crus.*—Weigert and Weigert-Pal sections of the crus cerebri were made. Fig. 36 shows that the pyramidal tract and the components of the crusta on either side of it were unaffected. A little higher up it can be seen that some of the fibres constituting the corticobulbar and corticopontine paths ("faisceau geniculé") which lie on the mesial side of the pyramidal path proper, are partly degenerated, as a result of the lesion at the genu of the internal capsule (left hemisphere). (*See* fig. 29.) The fibres and cells of the substantia nigra were possibly somewhat impaired, but there was no whole-

sale disappearance of these structures. The tegmentum generally was quite intact. The fibres of the red nucleus were apparently normal; they stained well, as can be seen in fig. 36, and the nucleus was of good size.

The cells of the red nucleus were examined with Nissl's method, as well as with hæmatoxylin-Van Gieson. They did not seem to be abnormal in any way, although it was noticed that a number of them were immediately surrounded by parasite glial cells, but not to a great extent.

(7) *Basal ganglia, internal capsule, subthalamic region.*—The two hemispheres were subjected to a complete examination by the method of serial sections. The right hemisphere, with the exception of the frontal and occipital poles, was cut up into slabs, 1 cm. thick. These were cut exactly at right angles to the *coupe d'élection*, and eight such slabs were impregnated with Müller's fluid, embedded and cut in celloidin, in complete series from before backwards. Every fourth section was stained either by Weigert's original stain or by Pal's modification. (*See* fig. 37.)

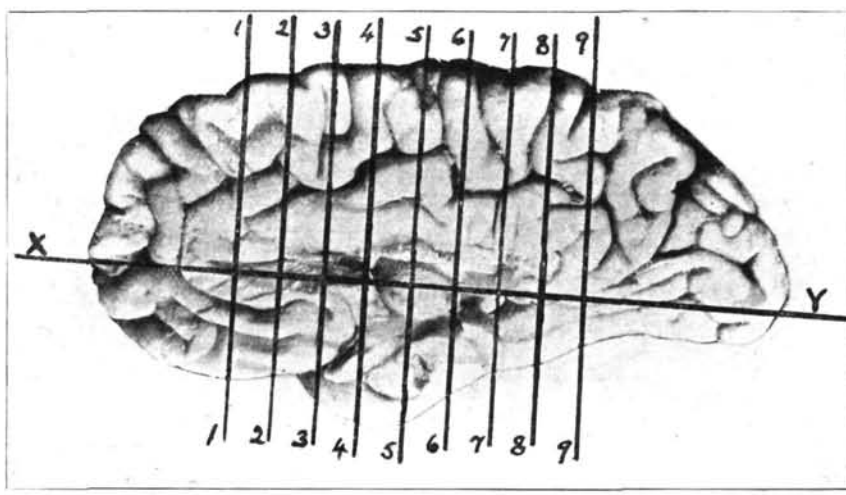

FIG. 37.—Shows method of subdividing the right hemisphere (Case 1) for examination in serial section. Each block is 1 cm. thick. X—Y is the line of Marie's *coupe d'élection*.

On the left side the hemisphere, with the exception of the frontal and occipital poles, was divided by a number of incisions exactly parallel to the *coupe d'élection* into a series of slabs 1 cm. thick. Of these, two were above the plane of the *coupe*, and two below. Fig. 38 shows their position in relation to the mesial aspect of the hemisphere. They were impregnated with Müller's fluid, embedded in celloidin, as in the case of the other hemisphere, and cut in complete serial section from below upwards. Each fourth section was taken, and stained as above.

Figs. 39, 40 were obtained when the right hemisphere was cut into divisions.

The first of these represents the naked-eye appearance of the anterior aspect of the slab at the line 4—4, and the second at the line 5—5 (of fig. 37). They portray, in a striking manner, the specificity of the lesion in progressive lenticular degeneration. They demonstrate the integrity of the optic thalamus, the relative integrity of the caudate nucleus, and the complete cavitation and destruction of the lenticular nucleus. The posterior end of the cavity, looked at from the front, as seen in fig. 40, is a striking object; the curious limitation of the lesion could not be brought out more convincingly.

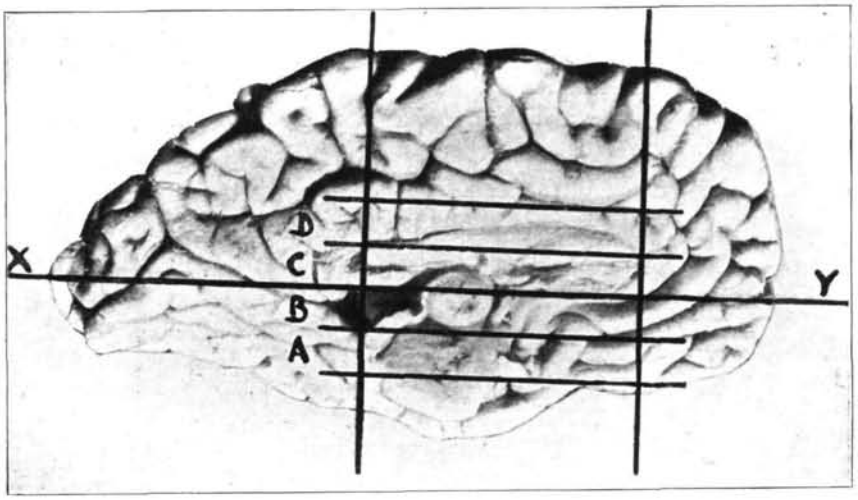

FIG. 38.—Slabs into which the left hemisphere (Case 1) was subdivided for the method of serial sections. Each is 1 cm. thick. X—Y as in fig. 37.

(*a*) *Description of the Appearances of the Lesions on Serial Section.*

(i) *Right side.*—The lesion began, on vertical transverse section, well towards the anterior extremity of the putamen, on a plane which passes through the tips of the temporal lobes, and at a level where the lenticular nucleus is continuous with the caudate round the anterior fibres of the internal capsule. Here a small hole made its appearance almost exactly in the middle of the putamen, and extended by a very narrow process into the internal capsule, the fibres of which it separated but did not appear to destroy. It looked as though the morbid process had extended along one of the "bridges" of grey matter that unite the putamen and the caudate across the capsule.

A few sections further back the cavity was about the size of a split pea, and had a very definitely thickened lining or wall to it, apparently not of recent formation.

At the level of the anterior tip of the globus pallidus (middle lenticular

zone) the lesion was still confined to the putamen. It was rather larger, but remarkably circular. The external capsule stained rather faintly towards its lower part, and was evidently thinned. The external medullary lamina of the lenticular nucleus had disappeared. The pencils of fibres passing mesialwards from the putamen were absent.

Further back, the lesion had spread into the middle zone and destroyed it completely, and had now its greatest diameter in a vertical direction. The

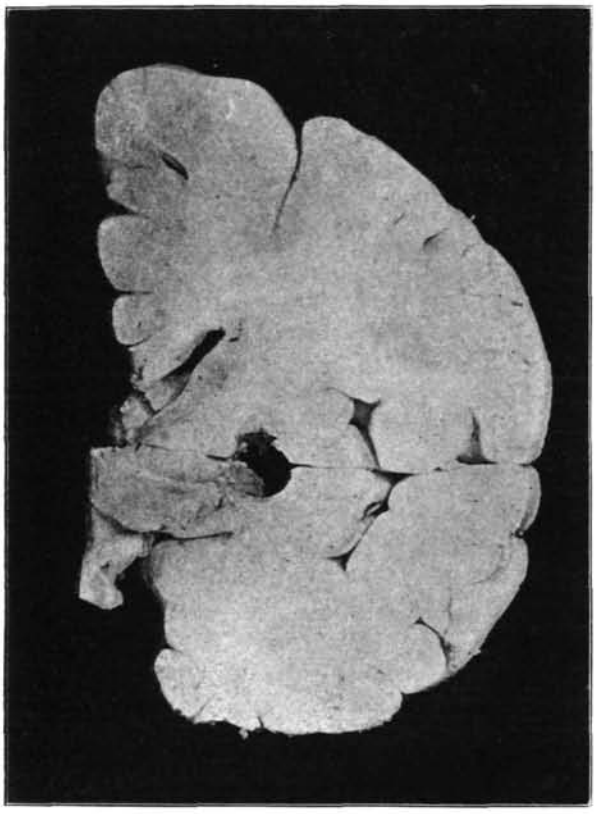

FIG. 39.—Corresponds to line 4—4 of fig. 37. Vertico-transverse section. Cavity in place of lenticular nucleus. Internal capsule intact.

internal medullary lamina could be distinguished, but it was considerably degenerated. The internal capsule was intact, however. The external capsule was somewhat attenuated, and the claustrum was affected, while the fibres of the upper convolutions of the island of Reil also seemed somewhat degenerated. The striothalamic fibres which cross the capsule to the external nucleus of the thalamus were found under a higher magnification to be greatly degenerated, and to be of irregular thickness and staining power; many were

moniliform. On the other hand, some of the bundles of fibres crossing the capsule were normal; probably some at least of these were coming in a reverse direction, from the thalamus. As for the globus pallidus—all that remained of it—its fibres were in a state of profound degeneration; they were twisted,

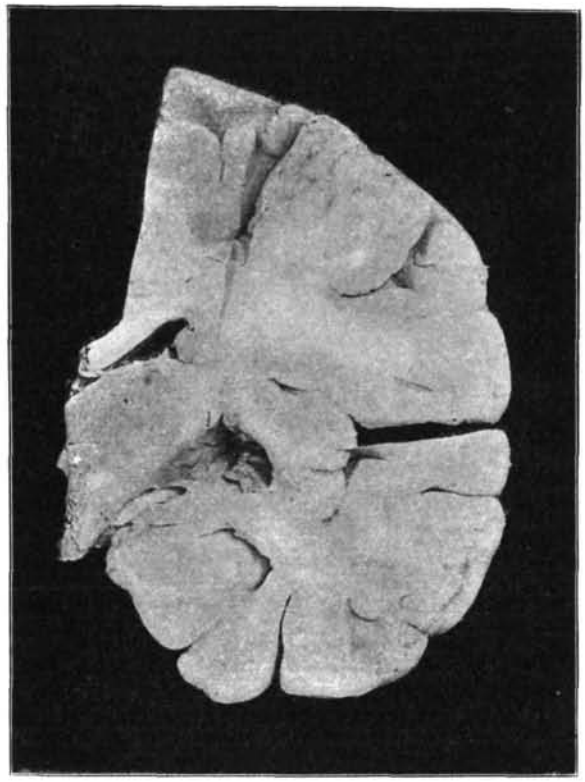

FIG. 40.—Corresponds to line 5—5 of fig. 37. Vertico-transverse section. Posterior end of lenticular cavity is well shown. Note the normal sized optic thalamus.

distorted, wavy, irregular in thickness; some showed a myelin sheath ending in a knot. Many stained badly. They were no longer arranged in close-set symmetrical bundles intersecting each other. The ansa lenticularis was found to consist of a few healthy fibres with many obviously degenerated fibres. All that was left of the putamen proper was a fibreless ring of degenerated tissue round the cavity.

A few sections further back the area of maximum disintegration was reached (fig. 41). The putamen and the middle lenticular zone were non-existent, and their place was taken by an irregular cavity which extended close up the internal capsule on the inner side, and to the claustrum on the outer. The internal lamina of the nucleus could be traced, but it was obviously degene-

rated; the fibres of the internal zone were greatly interfered with, and many of them were in a condition of decay. The internal capsule had some degenerated fibres in it, mostly towards that part of it which forms the genu. In the ansa lenticularis were a great number of defective fibres, along with some that seemed structurally to be normal. It could be traced, staining imperfectly,

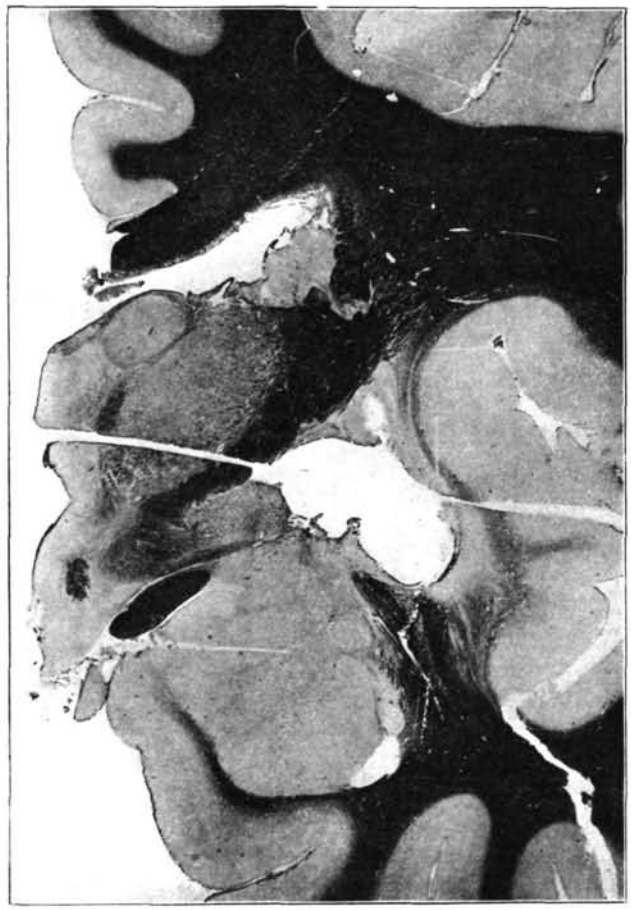

FIG. 41.—Vertico-transverse section No. 148. (Case 1.) Weigert-Pal. (About ½.) *See* description in text.

round the inner end of the capsule, towards the posterior and inferior part of the thalamus. The striothalamic fibres presented the same features as have already been noted. The external capsule was much thinned through the greater part of its extent. The fibres under the cortex of the upper convolutions of the island of Reil stained feebly ("capsule extrême"). The external medullary lamina of the optic thalamus was poorer in fibres than normally, and

the "zone grillagée" also was much less distinct than in the normal brain. The caudate at this level was somewhat shrunken and contained one or two minute areas of disintegration, and the lenticulo-caudate fibres were grossly degenerated.

The lesion came to an end by gradually narrowing to a point just short of the posterior inferior extremity of the putamen (fig. 42).

FIG. 42.—Vertico-transverse section No. 184. (Case 1.) Weigert-Pal. Posterior end of generated lenticular area. Note deeply staining internal capsule, also degeneration in posterior inferior part of thalamus (Forel's bundle, &c.).

A scrutiny of these serial vertico-transverse sections shows that there are certain secondary degenerations which require to be studied.

The ansa lenticularis, considerably degenerated, could be followed into the subthalamic region. Here it became difficult to trace; apparently some of its fibres joined others coming more directly across the capsule to the upper side of the corpus Luysii (strio-Luysian fibres), but its prolongation towards the capsule of the red nucleus could not be made out, presumably because of degeneration.

The corpus Luysii was undoubtedly smaller than normal and somewhat degenerated; under a high power the fine myelinated fibres contained in it were found to be thinned and reduced in number. Some were moniliform.

The lenticular bundle of Forel in the regio subthalamica was also degenerated, but not so much as the ansa, for a number of the fibres passing obliquely across the capsule from the inner zone of the globus pallidus and going to form part of Forel's bundle seemed normal. These were fibres arising from almost the only part of the lenticular nucleus that had escaped destruction. It is possible that some at least of these fibres were of subthalamic origin, passing in the reverse direction.

As regards the optic thalamus, it has been already remarked that the external medullary lamina was poorer in fibres than in the normal brain, irregular, and difficult to trace. The ganglion as a whole was not atrophic, and the fibres that skirt its nuclei were easily traceable. There was diminution of fibres, however, in the neighbourhood of the external nucleus.

The caudate nucleus throughout contained bundles of fine fibres passing down and across the capsule, and the majority of these appeared normal. They were, however, somewhat reduced in number. Towards the posterior part of the caudate rather more of these internuncial fibres were degenerated, including probably all that go from the putamen to the caudate.

The internal capsule stained with normal intensity all through the series of sections, except that it contained a few degenerated fibres in the immediate region of the genu. To all intents and purposes the corticospinal path was perfectly intact.

Türck's bundle was normal.

Retrograde degeneration, or any diffuse degeneration, is so difficult to follow in sections stained by the Weigert-Pal method that nothing can be said of any possible alteration in the corona radiata or in cortical fibres.

(ii) *Left side.*—The condition of affairs on the left side so closely resembled that on the right that a briefer description will suffice.

The lesion extended to the extreme lower and posterior portion of the putamen, behind the anterior commissure, and behind the spot at which the lenticulo-striate vessels enter the hemisphere to run vertically upwards. At a slightly higher level a cavity appeared also in the anterior portion of the same outer zone of the lenticular nucleus, and passing up it is found that where these two cavities united complete destruction of the putamen and of the outer part of the globus pallidus resulted, leaving a fragment of the inner part at its anterior end in which the nerve fibres that remained were all grossly degenerated (fig. 43). Where the lesion was at its maximum, about the middle of the putamen, considered vertically, was that little extension through the fibres of the internal capsule, at its genu, to which allusion has already been made. The little subsidiary cavity thus formed was lined by capsular fibres which stained deeply, but there is no doubt that a number in this section of the capsule were degenerated, for the degeneration could be traced. It was not, however, as pronounced as might have been expected from the

naked-eye appearance. There were also two very small holes in the outer part of the optic thalamus, close up to the capsule, as well as the other small punched-out depression which is seen in fig. 44. The lesion extended almost to the upper limit of the putamen, coming gradually to an end. A minute prolongation into the capsule, or rather through it, could be seen at the upper termination of the lesion.

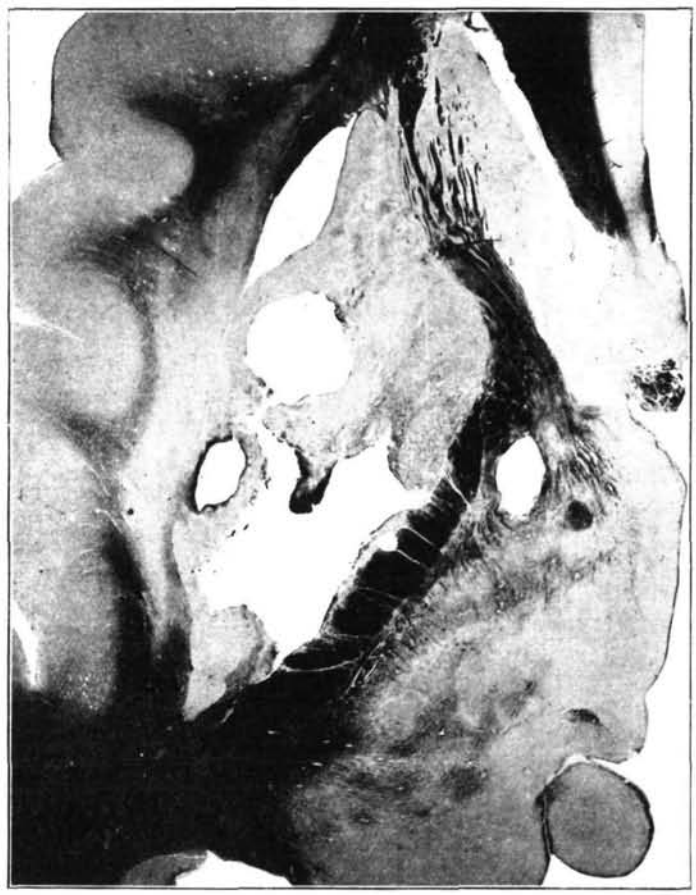

FIG. 43.—Horizontal section No. B 31, left hemisphere. (Case 1.) Weigert. (About ¾.) For description see text.

It is noteworthy that the external capsule was degenerated only towards the site of the maximum area of disease, for it was quite normal above, although the putamen was still completely softened. The convolutions of the island of Reil were more affected, i.e., their fibres stained less well towards the lower part of the island, but they did not appear to be softened or to have lost any substance. The claustrum was invaded apparently only in one place.

The internal capsule stained with normal intensity throughout, except that as the fibres converged to form the crus, in the subthalamic region, it could be seen that the genu bundle was partly degenerated. This degeneration, however, was not extensive. It has been already referred to. The caudate nucleus and optic thalamus were in much the same condition as on the opposite side. The optic thalamus was not directly affected at all, except for one or two very minute punched-out little cavities; it is noteworthy that no thalamic symptoms were present during life. In the horizontal sections the corpus Luysii was seen

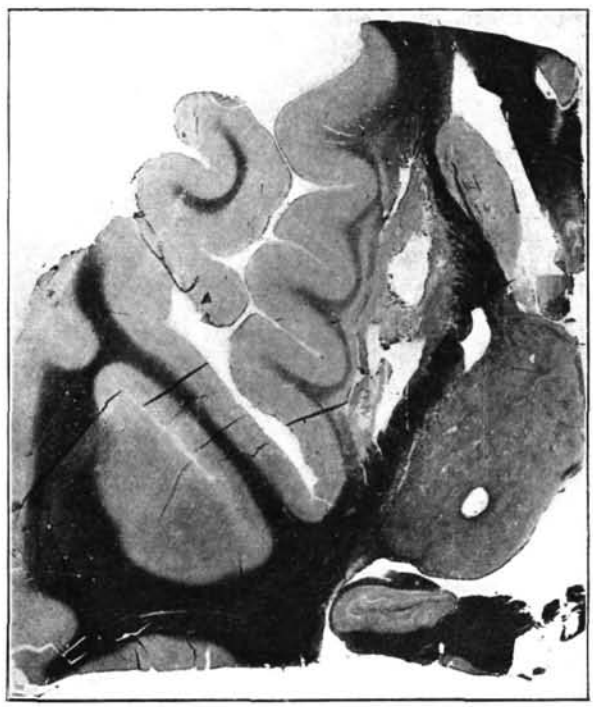

FIG. 44.—Horizontal section No. C 39. (Case 1.) Weigert. For description see text.

to be shrunken, and smaller than normal; the ansa lenticularis was degenerated, the lenticular bundle of Forel, and the strio-Luysian fibres which cross the pyramidal tract more or less obliquely, were partly degenerated, especially the former; amongst the latter there were a number of normal fibres; the red nucleus did not appear either to be smaller or to contain fewer fibres than in the normal brain. It is difficult to say whether the locus niger showed any pathological change; apparently not. As on the right side, the strio-thalamic fibres were much degenerated; the external medullary lamina of the thalamus was less marked than it should be; the "zone grillagée" of

Dejerine was scarcely distinguishable; the fibres in the neighbourhood of the external nucleus were considerably reduced in number.

In the Weigert-Pal sections, towards the base of the left hemisphere the shrinkage and cavitation of the outer lenticular segments, coupled with the gross degeneration of the densely packed fine fibres of the inner segment, and the secondary degenerations above referred to, the poor staining of the fibres of the convolutions of the island of Reil, the involvement of the external capsule—were all well seen.

(*b*) *Minute Anatomy of the Degenerated Area.*

Under a low power the walls of the cavity were seen to be composed of a thick interlacing network of neuroglial fibres, with neuroglia cells, degenerated myelinated fibres, diseased and fragmented blood-vessels and capillaries, all

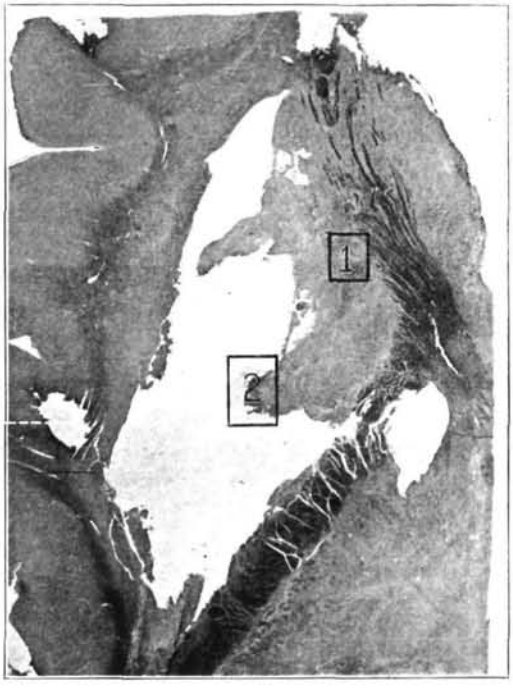

FIG. 45.—Photograph of maximum degenerated area (section imperfectly stained) to show situation of figs. 46 and 47 (1 = 47; 2 = 46).

mixed up inextricably. Along the margins of the cavity it was common to come upon such blood-vessels as are represented in fig. 46. It is noteworthy that while they were reduced to mere débris, none of them was

FIG. 46.—Margin of lenticular cavity. (× 60.) Hæmatoxylin-Van Gieson. (Corresponds to [2] of fig. 45.)

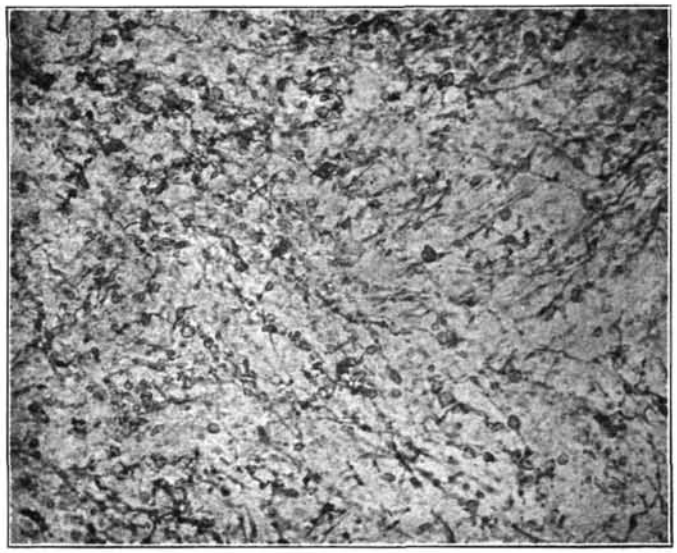

FIG. 47.—Degenerated fibres in globus pallidus. Weigert-Pal. (Corresponds to [1] of fig. 45.)

thrombosed or occluded. Not a single vessel in this condition was found in more than a score of sections. In some places the cavity wall was clean cut, firm, and evidently of old formation; in other places it appeared to be crumbling away. In the fragment of the globus pallidus that remained one or two nerve-cells could still be found, atrophic and staining deeply. Here the confusion of degenerated medullated nerve-fibres was at its maximum. (*See* fig. 47.)

In the small areas of putamen and globus pallidus that had not entirely succumbed the condition of the blood-vessels was investigated. One or two seemed to have undergone a sort of hyaline change, their coats staining in a homogeneous way, and being rather difficult to differentiate. In others the

FIG. 48.—Artery from globus pallidus. Hæmatoxylin-Van Gieson. Normal walls. (It has a plug of bacilli in its lumen.)

muscular and adventitial coats seemed thickened in proportion to the intima, which in no instance showed any sign of endarteritis. Many vessels were quite normal (fig. 48). No indication of small-cell infiltration was to be found round the vessels, in the lymphatic sheaths, or where the lenticular nucleus was degenerated. It is probable that some, if not most, of these changes in the vessels were of a regressive nature, and not the cause of the degeneration of the nucleus, but the result (fig. 49).

The sections of the middle cerebral artery and its branches, treated separately, showed no recognizable pathological change.

Under a higher magnification "Körnchenzellen" could be seen in the part of the globus pallidus that was left, but they were not present in numbers.

(8) *Cortex cerebri.*—The cortex cerebri was investigated by Nissl's method, as well as with hæmatoxylin-Van Gieson. Pieces were taken from various parts of the motor area on both sides, as well as from frontal, occipital, and temporal lobes.

In the precentral gyrus, certain changes were found, more obvious in some sections than in others. While the great majority of the Betz-cells were

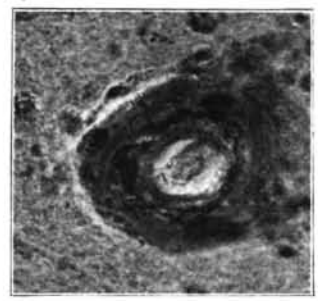

FIG. 49.—Degenerated blood-vessel from near margin of lenticular cavity. (Case 1.) Hæmatoxylin-Van Gieson. Thickening of middle and outer coats. Lumen patent. No small-cell infiltration. The changes are probably secondary to the lenticular degeneration.

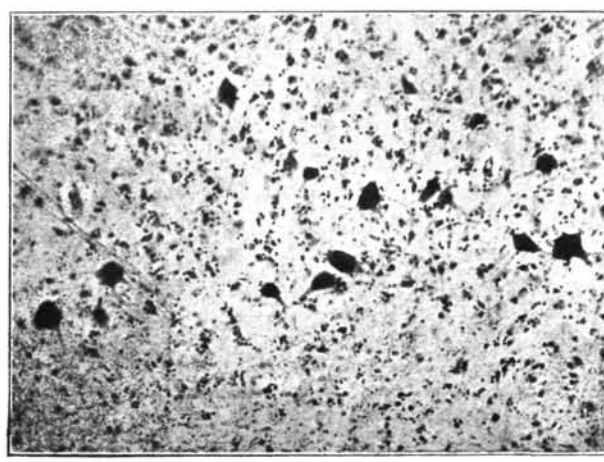

FIG. 50.—Oblique section from right leg centre, paracentral lobule (Case 1). Nissl. Normal Betz-cells.

normal, a few showed pigmentary degeneration, with some tigrolysis, presumably a change of a fairly chronic regressive type. Their numbers were not diminished to any extent. In the shoulder area the Betz-cells were practically all normal. In sections from the leg centres the appearances were more or less normal. Thus in fig. 50 (right leg centre) it can be seen that

the Betz-cells are of normal size, shape, and staining properties. The same was the case with the left leg centres. The other layers of the cortex in the precentral gyrus could be readily distinguished and did not seem deficient in any way.

In view of the almost complete helplessness of the patient, and in view of the spasticity, tremors, and contractures, the practically normal condition of the cyto-architectonic structure of the motor area, and the integrity of the corticospinal tracts, are facts of great importance.

The cortex of other parts of the brain showed changes so slight that it is difficult to know what importance to attach to them. Occasional pigmentary degeneration of pyramidal cells occurred, but there was no wholesale disappearance of cells, or confusion of cell layers. The cortex was of good depth everywhere.

In no one of many scores of sections examined was there any trace of small-cell infiltration of cortical vessels, so that the pathological picture was very different from that of dementia paralytica.

In sections of the motor cortex stained by Pal's method for myelinated fibres, it was seen that the tangential layer of fine fibres was considerably reduced, but the supraradiary and intraradiary networks were not altered to any extent.

Microscopical Examination of other Organs.

(1) *Liver.*—The histological methods utilized were hæmatoxylin-eosin, hæmatoxylin-Van Gieson, carbol gentian violet, Weigert's stain for elastic tissue, Sudan III for fat.

Under a low magnification the appearance represented in fig. 49 was met with. Numerous islets of liver-tissue, not a few of which did not contain more than one or two liver units, while others were much larger, were separated from each other by wide strands of cirrhotic tissue, which in some places was mainly fibrous, in others very cellular. Occasionally a few isolated liver-cells, as was determined by the method of serial sections, were noted to be surrounded by cirrhotic strands. There was little indication, however, of any intralobular spread of connective tissue, so that the monocellular type of cirrhosis was not in evidence. In the more cellular areas of cirrhosis abundant bile-ducts ramified in all directions.

The condition of the liver-cells was highly irregular. Many lobules appeared to be normal, the columns of cells being symmetrically radiate, staining well and of good size. In other nodules scarcely a single normal cell was found; many were in a necrotic state, shrunken and staining homogeneously a brighter tint with eosin than normal cells. Everywhere there were evidences of fatty degeneration. On the other hand, more particularly towards the periphery of some of the nodules, regeneration of liver-tissue was actively proceeding. Thus it was common to find the nuclei of the cells enlarged; some were dumb-bell-shaped and evidently about to divide by

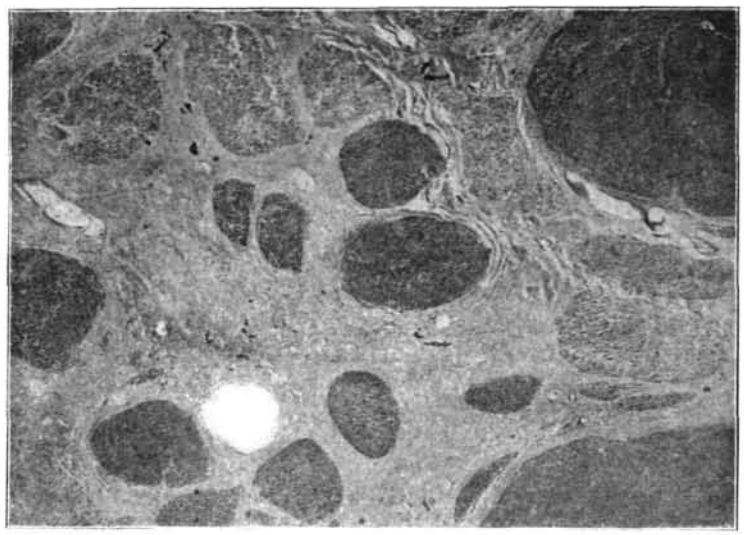

FIG. 51.—Liver (Case 1). Hæmatoxylin-Van Gieson. Irregular size of liver-nodules. (× 20.)

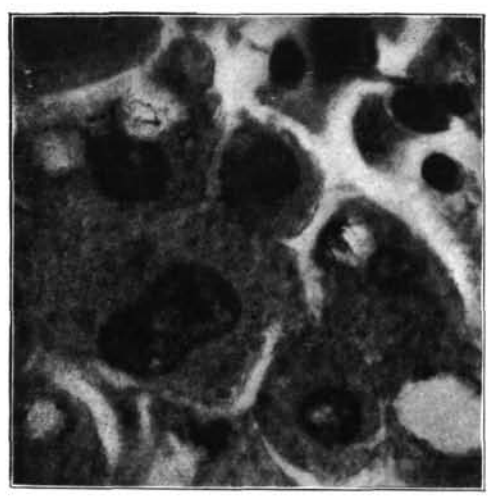

FIG. 52.—Liver-cell dividing by an amitotic process. Hæmatoxylin eosin. (× 1,000.)

an amitotic process (fig. 52). Other cells were doubly nucleated. In the regenerating areas metachromatic staining of the nuclei was common. No definite mitotic figures were seen; apparently this form of multiplication is much less frequent than the other.

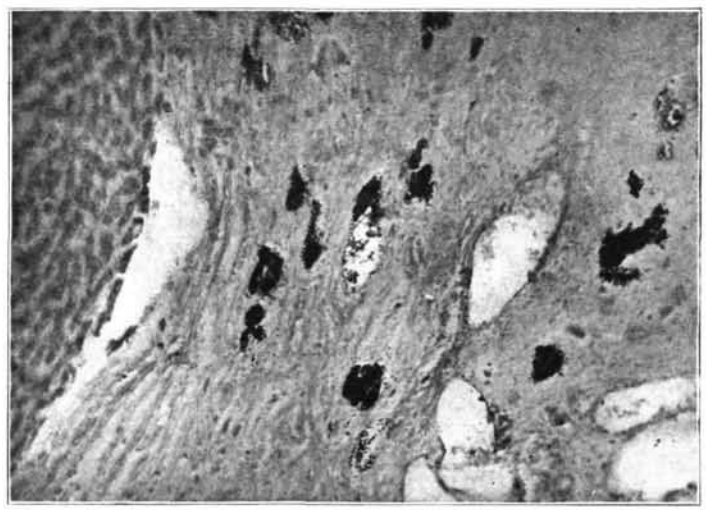

FIG. 53.—Clumps of bacilli in cirrhotic liver-tissue (Case 1). Carbol gentian violet. (× 60.)

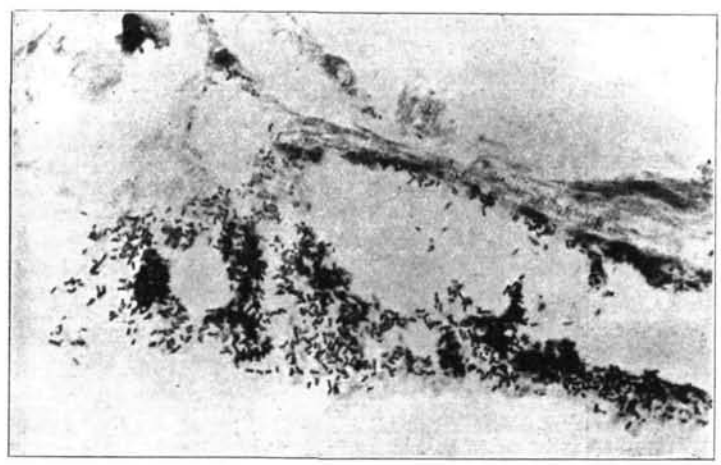

FIG. 54.—Bacilli in neighbourhood of portal tract (Case 1). Carbol gentian violet. (× 750.)

The portal tracts and vessels of the organ did not show any particular alteration beyond an increase in connective tissue round the tracts. There was no indication of inflammatory processes, in particular, no small-cell

infiltration. A few plugs of inspissated bile were found. There was no sign of any obliteration of bile-ducts.

(2) The *suprarenals* did not present any obvious morbid change.

(3) The *thyroid* showed certain regressive changes in the shape of interstitial overgrowth and diminution of colloid.

There remains to be described only one other pathological condition, but this is a widespread one. In every organ examined, particularly in the liver, in the gall-bladder walls, and in the central nervous system, bacterial invasion was acute. Clumps of short bacilli, structurally rather like the *Bacillus coli communis*, were seen everywhere in sections of the liver, and were found plugging the vessels of the degenerated lenticular area (*see* fig. 48), in the cortex cerebri and cerebelli, and in the spinal cord. The appearances presented in the liver are reproduced in figs. 53 and 54. The widespread nature of the condition suggests a terminal infection, which, it is known, can take place with extraordinary rapidity. It is probable that the infection was from the alimentary canal, as the patient had neither bed-sores nor cystitis. It is difficult to believe that the infection is of any special pathogenic significance.

Résumé of the Pathological Findings in Case 1.

The brain is of good size, shape, and weight. The cerebral gyri are not atrophic, are of normal convolutional pattern, and present no obvious morbid appearance. The membranes are to all intents and purposes normal. The cerebral blood-vessels are not thickened or occluded, and show no patches of disease in their walls.

On Marie's *coupe d'élection*, the eye is at once caught by a complete bilateral and symmetrical destruction of the lenticular nucleus. In place of the latter, on either side, and more especially in place of its outer and middle zones, is an elongated cavity, measuring $2\frac{1}{2}$ cm. long by $1\frac{1}{4}$ cm. wide, with dark-coloured crumbling walls, extending from the anterior to the posterior limit of the putamen, and from its extreme lower extremity almost to its upper limit. Only a small piece of the inner zone of the globus pallidus remains. Compared with this utter degeneration of the lenticular nucleus, the optic thalamus and the caudate nucleus are well preserved, except that in the former, on the left side, there is a small punched-out hole towards its posterior part, and the latter is on both sides a little shrunken, and less full and rounded than in a normal brain. The degenerated area extends close up to the internal capsule on both sides; on the right this seems quite intact throughout, although it is found to be somewhat undermined; on the left there is a small prolongation of the cavity across the genu of the capsule, the fibres of which are separated rather than destroyed.

Microscopically, however, there is some descending degeneration in the genu fibres.

The external capsule is thinned on both sides, and degenerated in its middle third; the claustrum is very slightly invaded on the left side; the cortex of the island of Reil is well preserved on both sides, although microscopically there is some degeneration of the subcortical fibres of its convolutions towards its posterior part.

The white matter of the cerebral hemispheres is normal. The cortex is practically normal; in particular the origin of the pyramidal tracts in the Betz-cells of the motor area is carefully examined, and the great majority of the latter are found to present no morbid appearance, although some show chronic degenerative changes.

With the exception of the slight descending degeneration in some capsular genu fibres on the left side, the pyramidal tracts stain normally throughout, and, followed from the motor cortex through the capsule, crus, pons, medulla and cord, are perfectly normal.

On the other hand, the extrapyramidal system from the lenticular nucleus, viâ the ansa lenticularis, to the red nucleus, is degenerated on both sides; the lenticular bundle of Forel is partly degenerated, as are a large number of the strio-Luysian fibres on both sides; the corpus Luysii is smaller than normal. The cells of the red nucleus do not appear changed, nor does the nucleus seem altered in its fibre-content. The striothalamic fibres are degenerated.

The external medullary lamina of the optic thalamus, the "zone grillagée," and the outer part of the thalamus generally, are to a certain extent altered.

The pons and medulla, and the cerebellum, are not the seat of any change that can be recognized microscopically.

The nuclei of the cranial nerves are unchanged, except for slight alterations of secondary significance.

The spinal cord (cells and fibres) is normal, except for certain slight alterations, also of secondary significance.

The same is true of the muscles.

The liver is in an advanced state of cirrhosis; the type is mainly multilobular, but some monolobular cirrhosis is found. In the cirrhotic tissue abundant bile-ducts ramify. The liver-cells are in many instances normal, others are necrosed, many show fatty infiltration and degeneration, others are actively regenerating.

The spleen is not enlarged. The thyroid shows interstitial changes.

There are evidences in all the organs examined, particularly in the liver and nervous system, of a terminal bacterial infection.

Case 2.—The autopsy was performed by Dr. W. H. B. Stoddart and myself on March 4, 1907, thirteen hours after the death of the patient.

The body was greatly emaciated, but there were no bruises or bed-sores. The skullcap and the dura mater with its veins and sinuses presented no abnormality. The cerebral arteries at the base of the brain were all normal, patent, and showed no visible thickening or patchy degeneration. There was

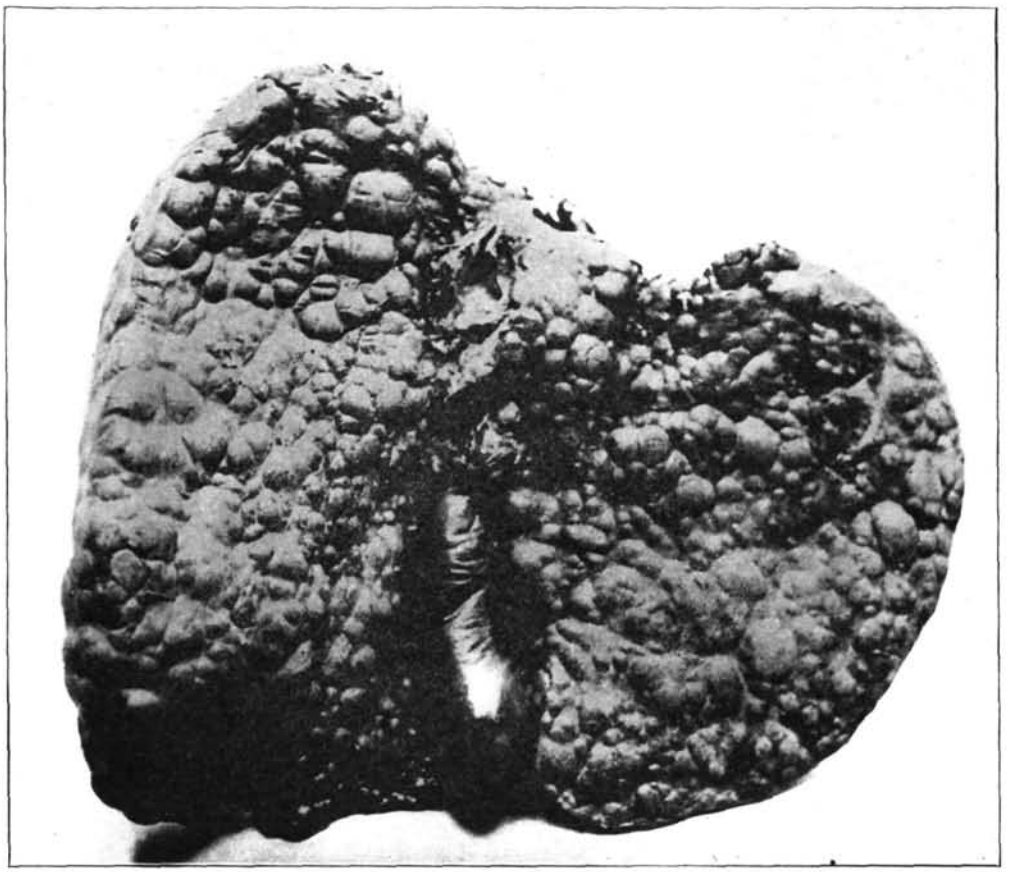

FIG. 55.—Liver, under surface (D. P., Case 2).

excess of cerebrospinal fluid on opening the membranes, especially in the subarachnoid spaces. The brain looked œdematous, and the convolutions somewhat separated from each other. It weighed 1,275 grm. The pia-arachnoid appeared slightly thickened in one or two areas.

The bronchial vessels were congested, and there were several patches of pneumonic consolidation scattered throughout both lungs, the largest patch being at the apex of the lowest lobe of the right lung. The heart was normal.

The spleen was enlarged, and weighed 312 grm., but it showed no obvious morbid appearance on section. The kidneys were normal.

The liver presented a remarkable appearance. It was in an advanced state of multilobular cirrhosis, being subdivided up into spherical portions of liver substance about the size of small hazel-nuts, held together by bands of cirrhotic tissue. It was firm, and tended to preserve its shape. Its weight was 1,392 grm.

Figs. 55 and 56 show the naked-eye appearances of that organ. One of

FIG. 56.—Liver, transverse section (D. P., Case 2). Natural size. The general character of the cirrhosis and the varying appearance of the nodules are well shown.

them (fig. 56) was taken after the liver had been in formalin for about twelve months, and it shows the appearance on transverse section. The irregular size of the nodules and the difference in their colour are well brought out. Some were much darker than others, while many looked somewhat mottled. The strands of cirrhotic tissue were notably slender in comparison to the dimensions of the nodules which they enclosed. There was some thickening along the portal tracts. The capsule of the organ was slightly thickened.

When it was removed from the body it was not noted to be bile-stained; the gall-bladder was in a normal condition.

Macroscopical Examination of the Central Nervous System.

Owing to an unfortunate accident the nervous organs were rendered almost useless for certain methods of investigation, so that to some extent it must be considered incomplete. What I am able to describe, however, will be sufficient to class the case *in toto* with No. 1 and No. 3.

The brain, when stripped of its membranes (which were not adherent) was found to be of good size, shape, and convolutional pattern. On a transverse horizontal section through the right hemisphere, the putamen was found to be darker in colour than usual; it was shrunken and soft. There was not, however, any gross loss of substance—i.e., no cavitation. The globus pallidus also appeared somewhat shrunken, while the optic thalamus, the caudate nucleus, and the internal capsule were normal. I am unable to say what the condition on the left side of the brain was, and whether there was any similar degeneration of the outer zone of the lenticular nucleus. On the right side the internuncial fibres from the outer to the middle zone of the nucleus were almost entirely absent, and the outer lamina was not readily distinguishable. The fine fibres of the caudate, however, could be seen easily. The external capsule and the white and grey matter of the convolutions of the island of Reil presented no obvious morbid appearance.

No other change was demonstrable on this section by Marie's *coupe d'élection*. The cerebral cortex appeared to be of good depth everywhere, with the possible exception of the first and second frontal convolutions, where it may have been a little thinned. The white substance of the hemisphere presented no abnormality. There was no hydrocephalus, and no ependymitis.

The pons, medulla and cord, and the cerebellum, looked quite normal.

Microscopical Examination of the Nervous System.

(1) The *muscles* and the *peripheral nerves* were not examined.

(2) *Spinal cord.*—The methods of staining employed were Weigert-Pal, Nissl, and hæmatoxylin-Van Gieson.

The meninges were everywhere normal. There was no trace of pachy- or lepto-meningitis: in particular, there was no small round-cell infiltration of any sort. The spinal vessels, both intra- and extra-medullary, were normal, and showed no sign of endarteritis.

The spinal cord, from the point of view of its myelinated fibres, was normal. In particular, there was no trace of any degeneration in the pyramidal tracts. The medullated fibres of the grey matter of the cord were likewise normal, if perhaps a little sparser.

Examined by Nissl's method, the cells of the anterior horns were found to be present in good numbers, to stain well, and to preserve a normal size and

shape in the great majority of them. Some were slightly shrunken and elongated, staining unusually deeply, but remaining nucleated. Others were in a state of commencing pigmentary degeneration, but there were not any, as far as was noted, that showed an acute form of degeneration associated with excentricity of the nucleus and pulverization of the tigroid substance round it.

(3) *Medulla, pons, and cerebellum.*—The same methods were employed for the examination of these structures as for the cord.

With the Weigert-Pal stain no defect was to be seen in the corticospinal tracts anywhere. They stained deeply, and were not degenerated in any way. The transverse sections of the medulla (fig. 57) and pons that were examined seemed normal in all respects. Similarly with the cerebellum, its nuclei and peduncles did not show any deviation from the normal.

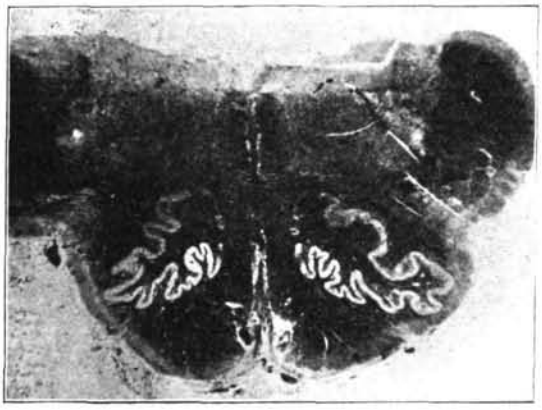

FIG. 57.—Medulla (Case 2). Weigert-Pal. (The marginal ring of "bleaching" is due to the piece having been accidentally left in absolute alcohol.)

The nuclei of the cranial nerves, especially the facial and the hypoglossal, showed no pathological change by Nissl's method. The cells were present in good numbers, with normal staining reactions.

(4) *Crus cerebri.*—The pyramidal path in the crus was unimpaired. The red nucleus was not altered in its fibre-content, nor in its cells, as seen when stained with hæmatoxylin-Van Gieson.

(5) *Basal ganglia and internal capsule.*—The appended description applies to the right side only, and is of necessity somewhat incomplete. The histological methods utilized were the same as for the cord.

In the degenerated right putamen there was considerable overgrowth of neuroglial tissue, forming a fairly thick feltwork; it was in some places sparse and evidently breaking down. Great numbers of glial nuclei were to be seen. In the degenerated area there were no signs of inflammatory reaction.

The important feature of sections through the lenticular nucleus was the dearth of nerve-cells, both in the putamen and the globus pallidus, but particularly in the former, which was almost cell-less. The blood-vessels were neither thickened nor obliterated, but stood out prominently, usually with enlargement of the Virchow-Robin space, and were often apparently somewhat dilated, possibly a little thinned (fig. 58). There was no trace of

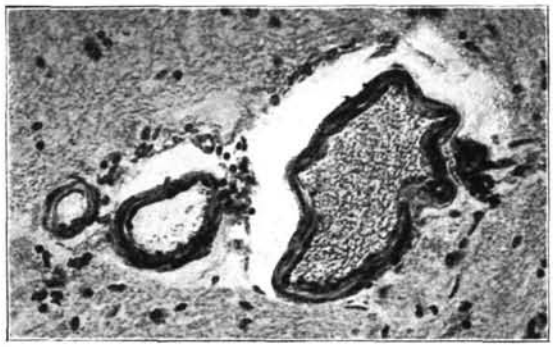

FIG. 58.—Vessels from the right putamen (Case 2). Hæmatoxylin-Van Gieson. Normal walls. No small-cell infiltration.

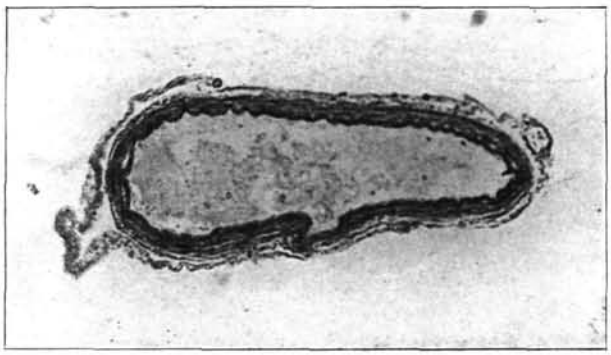

FIG. 59.—Transverse section of a lenticulo-striate artery, removed from degenerated area and cut separately (Case 2). Hæmatoxylin-Van Gieson. The vessel is, if anything, thinned. No trace of endarteritis. (× 150.)

endarteritis; the intima was unaltered. Nor was there any thickening of any of the other coats. Fig. 59 represents a transverse section of one of the lenticulo-striate arteries, removed from the degenerated area and cut separately. Endarteritis was conspicuously absent.

The caudate nucleus showed a slighter degree of the change that was found in the putamen; there seemed to be an increase of glial nuclei, and fewer

nerve-cells than in the normal nucleus. But the changes were slight. From the point of view of cells and fibres, the optic thalamus was practically normal.

The internal capsule throughout stained in normal fashion, and was neither atrophied nor hypertrophied. Both its anterior and its posterior limbs were intact. The fibres that cross the internal capsule, running between the globus pallidus and the optic thalamus (striothalamic), were mostly normal. They stained well, and were not diminished in numbers. Some, however, were degenerated. The inner lamina, between the middle and inner zones of the lenticular nucleus, was well developed, but the fibres that pass mesially from the putamen to the globus pallidus were greatly diminished in number, and to a great extent degenerated, except at its anterior and posterior extremities. The external capsule did not seem to be involved in the disease, and the fibres of the white matter under the convolutions of the island of Reil were normal, except in one place, opposite the centre of the putamen, where they did not stain well with Weigert-Pal.

In this case, unfortunately, it was impossible to examine further the lower portions of the degenerated area, so that the condition of the ansa lenticularis is not known, nor of the structures in the subthalamic region.

(6) *Cortex cerebri.*—Pieces were taken from both sides of the brain, including in particular the motor area, with both the precentral and the postcentral convolutions.

It may be said at once that from the cyto-architectonic point of view no definite changes could be made out. The Betz-cells of the motor area were easily recognizable, present in quantity, and not altered in staining reactions or in morphological characters, except that a few showed commencing pigmentary degeneration. The cells of the pyramidal layers did not appear to be altered, though round many of them parasite neuroglial cells were to be seen. The depth of the motor cortex was not appreciably different from the normal brain.

The cortex in the other areas examined did not show any pathological change that need be specified.

From the myelo-architectonic point of view only the fibre-content of the motor area was investigated, and it proved to be normal, with the exception of considerable diminution in the tangential layer, and to a less extent of the supraradiary network.

Nowhere in the cortex were the vessels surrounded by small-cell infiltration, nor was there any sign of increased neuroglial growth.

Microscopical Examination of other Organs.

The only other organ subjected to examination was the liver, which was stained with hæmatoxylin-eosin, hæmatoxylin-Van Gieson, Weigert's elastic tissue stain, and Sudan III.

Under a low power the liver-nodules presented a varied appearance. Some

contained one or two lobules only; the majority contained as many as eight or twelve; some were evidently in full functioning power, as the columns of liver-cells were normal; others were totally degenerated and changed into a mass of fat-granules. In many places in the cirrhotic tissue immense numbers of small connective tissue cells, and great numbers of so-called new bile-ducts, were to be seen. The cirrhotic tissue was slender and nowhere looked very fibrous. In some places there were delicate strands of connective tissue passing between groups of liver-cells. The cells themselves, under a higher magnification, were found in most lobules to stain normally, but in areas where active regeneration was taking place—and of this there was abundant evidence —metachromatic staining was noticed. Regeneration was shown by the presence of enlarged or doubled nuclei; sometimes amitotic division was seen, but no mitotic figures.

There was no special feature to be noticed in the sections stained by Weigert's elastic tissue stain. The picture given with the Sudan III sections was very striking, and explains the irregular coloration showed in the naked-eye photograph reproduced as fig. 56.

Résumé of the Pathological Findings in Case 2.

The brain is of good size and shape, and its convolutional pattern is normal. There is no indication of atrophy of the gyri, except that possibly the cortex of the frontal convolutions is a little thinned. This, however, if present, is so slight as to be negligible. The white matter of the hemispheres shows no abnormality. The membranes are normal, except that in one or two places the pia-arachnoid is a little thickened. The cerebral blood-vessels present no deviation from a normal state. The pons, medulla, and cord look normal.

On section the right lenticular nucleus is seen to be in a definite state of degeneration; it is atrophic in its outer zone or putamen, shrunken, discoloured, looks friable, and feels soft. There is not, however, any gross cavitation. The globus pallidus does not appear to be impaired beyond being perhaps a little smaller than usual; the external capsule is normal. The degeneration in the putamen occupies its whole breadth, but leaves a small portion anteriorly and posteriorly which seems intact. Microscopically there is marked neuroglial sclerosis, overgrowth of glial nuclei and fibres, almost complete disappearance of nerve-cells from the putamen, and considerable involvement of the internuncial fibres from the outer to the inner zones of the lenticular nucleus.

The arteries of the affected area do not show any change, except that they are, if anything, dilated and thinned, in some instances at

least. There is no endarteritis of any vessel, and no small-cell infiltration.

The internal capsule, the optic thalamus and caudate nucleus are normal throughout, except for slight commencing changes in the last of these.

The motor cortex is normal, and the pyramidal tracts, examined from the Betz-cells of the cortex to the anterior horn-cells of the spinal cord, are likewise normal. There is no degeneration in the cord, by any method.

The liver is profoundly cirrhotic, though the bands of cirrhosis are relatively slender; many nodules are reduced to masses of fat, but others are actively regenerating. Numerous bile-ducts course in the cirrhotic tissue.

Case 3.—The autopsy was performed by myself at 7.30 p.m. on the evening of September 21, 1910, twenty-seven hours after death. As the body had been kept in the open air, the sanatorium being at a considerable altitude and the nights very cold, it was in an excellent state of preservation.

Post-mortem lividity was marked. The limbs remained very rigid. There were fairly large superficial abrasions over the heels, trochanters, and sacrum. The body was profoundly emaciated, being reduced almost to skin and bone. The outlines of the muscles, wasted as they were, were unusually distinct beneath the skin. On opening the calvarium the dura was not adherent, nor was it obviously thickened or discoloured. On its being cut open the sub-arachnoid spaces and cisterns were found to be greatly distended with fluid. As a result the brain looked œdematous and the outlines of the convolutions were indistinct through the distended membranes. Over one minute spot at the upper end of the left Rolandic area the dura was adherent to the tissues underneath. The cerebral veins were greatly distended everywhere. Over the base of the brain the arachnoid appeared somewhat thickened, and a little opaque, especially across the pons and the interpeduncular space. Elsewhere that membrane seemed normal, with the possible exception of the portion that covered the anterior parts of the temporal lobes, which also appeared rather opaque. As the brain was being taken out my impression was that the pons was rather small in proportion, and that the cranial nerves were rather slender.

The brain and cord were at once immersed in a 10 per cent. solution of formalin.

The pituitary gland, thymus, left lobe of thyroid, left suprarenal body and left kidney were removed for subsequent examination. The thyroid appeared to be of normal size, and the other organs mentioned above presented no obvious alteration to the naked eye. The spleen was slightly enlarged, felt firm, and on section showed no deviation from the normal, except that it was congested.

The heart and lungs were normal, except that the latter were somewhat

congested. There were a few ounces of clear fluid in each pleural cavity, but no adhesions.

The liver presented a striking appearance, which is seen in figs. 60 and 61. It was of medium size, of good shape, and weighed 1,450 grm. It was firm and preserved its shape well when removed from the body. When examined it was at once seen to be in a state of profound cirrhosis; the dome-like upper surface and the under surface were not smooth, but subdivided up into innumerable small raised nodules, between which were narrow lines where

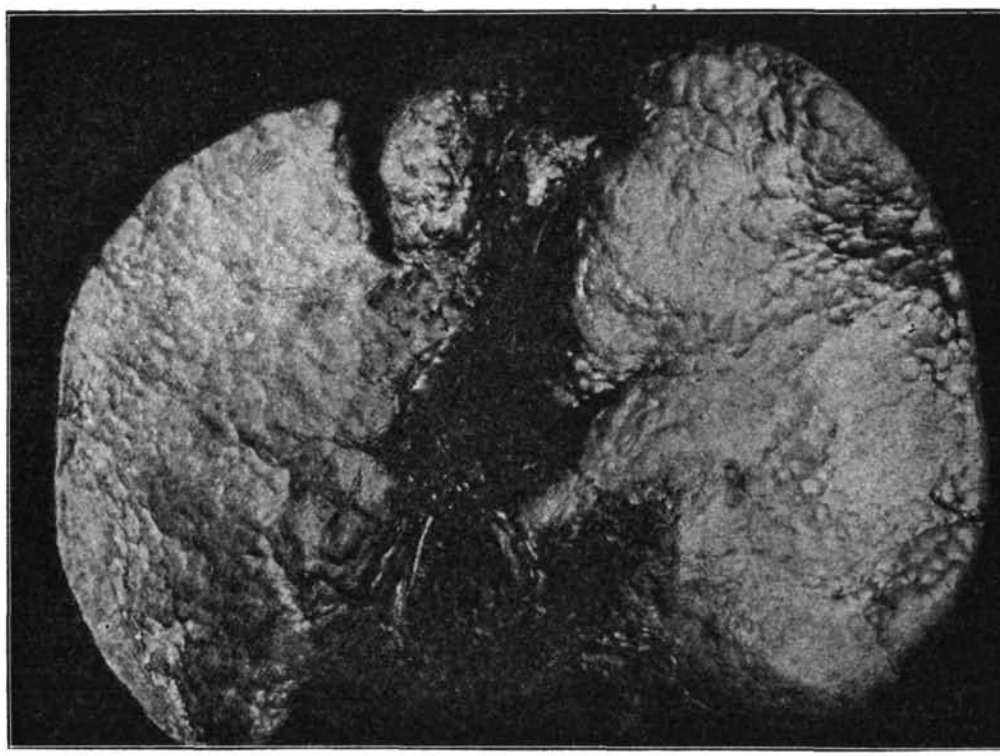

FIG. 60.—Liver (E. P., Case 3). Under surface.

the surface was depressed, corresponding to bands of cirrhotic tissue. The average size of the nodules was perhaps that of a threepenny-piece, but they varied considerably. In some places they were more evident and more closely set than in others. There were no signs of hepatitis; the capsule was not definitely thickened anywhere, and there were no adhesions to the surrounding viscera. The organ was, if anything, rather lighter in colour than usual; it was not bile-stained, nor was the coloration patchy or irregular. Its appearance on transverse section was equally striking. From one side to the other it was subdivided into more or less circular or oval nodules, or islets, most

of which were about the same size, and were separated from each other by narrow cirrhotic strands. In one or two places the cirrhosis approximated to the monolobular type, but it was far more characteristically multilobular.

There was no ascites.

The following muscles were taken for subsequent microscopical examination: muscles of the left thenar eminence, left flexor sublimis digitorum, right flexor carpi ulnaris, right biceps, right supinator longus.

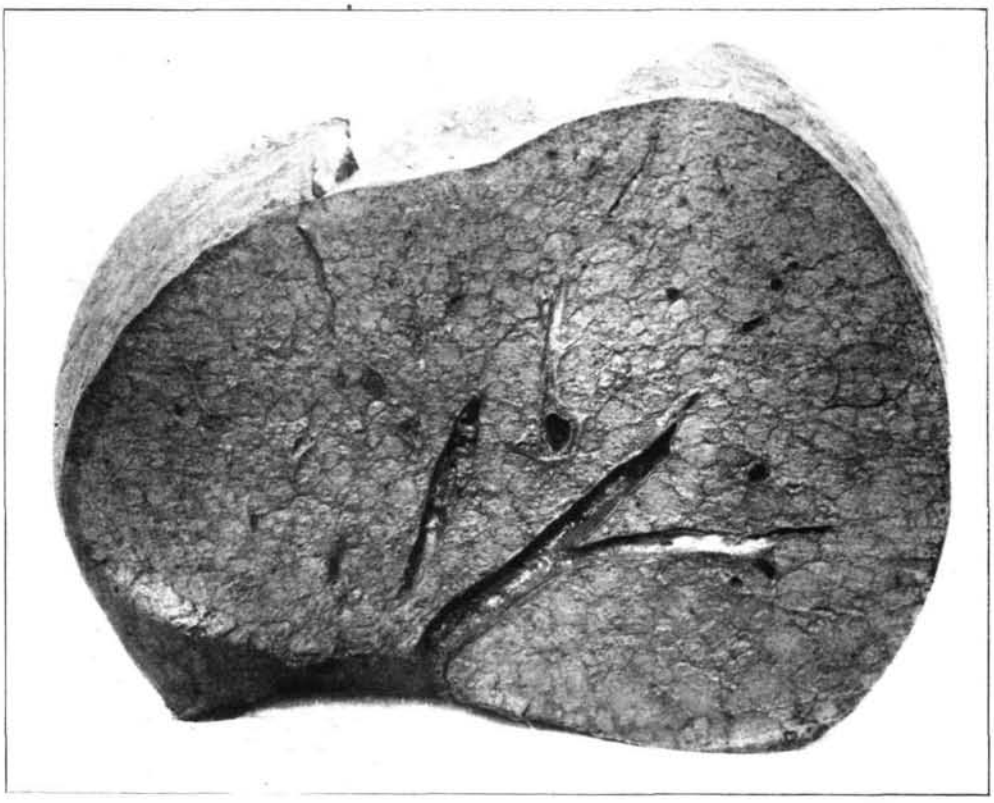

FIG. 61.—Liver, transverse section (E. P., Case 3).

MACROSCOPICAL EXAMINATION OF THE BRAIN AND CORD.

After hardening in formalin the brain was stripped of its membranes. The middle cerebral artery and its branches, as far as practicable, were removed for microscopical examination, from the left side. The weight of the brain thus stripped was 1,245 grm.; the cerebrum alone weighed 1,080 grm., the cerebellum, pons and medulla together 165 grm.

The cerebral hemispheres were well developed and of good convolutional

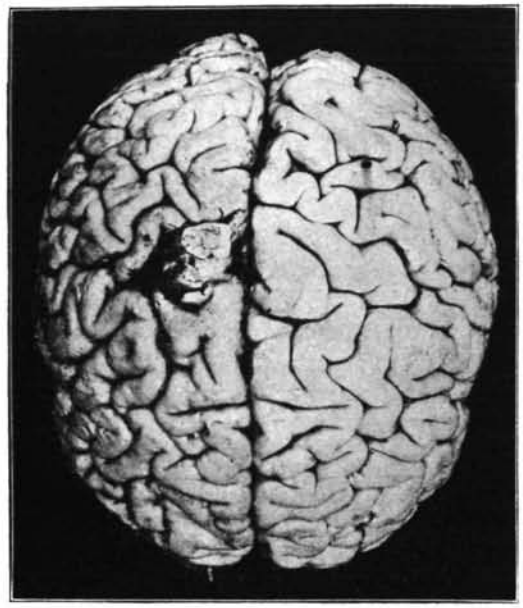

FIG. 62.—Upper surface of cerebrum (Case 3). (The membranes have been left at one spot over the right Rolandic area for histological purposes.)

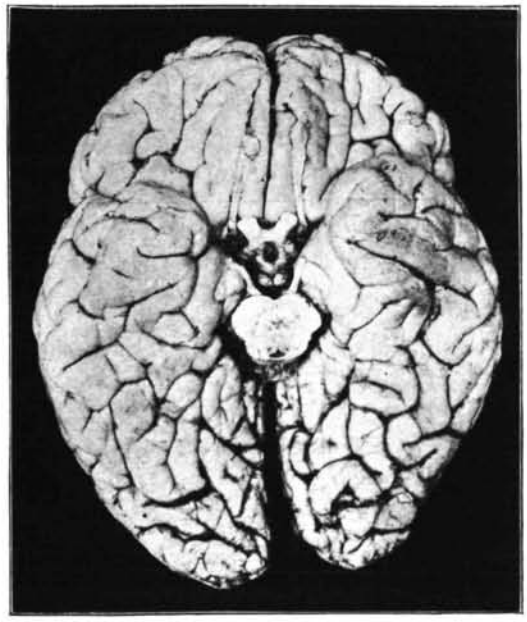

FIG. 63.—Under surface of cerebral hemispheres (Case 3). Cerebellum, pons, and medulla have been removed.

pattern, as can be seen from figs. 62, 63, and 64. There was no obvious atrophy of any of the gyri, and no undue spacing between them. The corpus callosum was divided by an incision in the mesial plane, and then each of the hemispheres was cut by Pierre Marie's *coupe d'élection*. The appearance of the sections is given in fig. 65.

Right side.—The posterior two-thirds of the putamen in its complete transverse extent, and to a less degree the corresponding part of the middle zone of the lenticular nucleus, were the seat of an obvious softening. The substance of the nucleus was discoloured, friable, pitted, as it were worm-eaten. There were a number of small holes in it, evidently related to blood-vessels; many were clean cut and empty, and round these—i.e., in the area where these were—the degeneration of the nucleus seemed at its maximum. The minute vessels which remained stood out from the surface of the section, were patent,

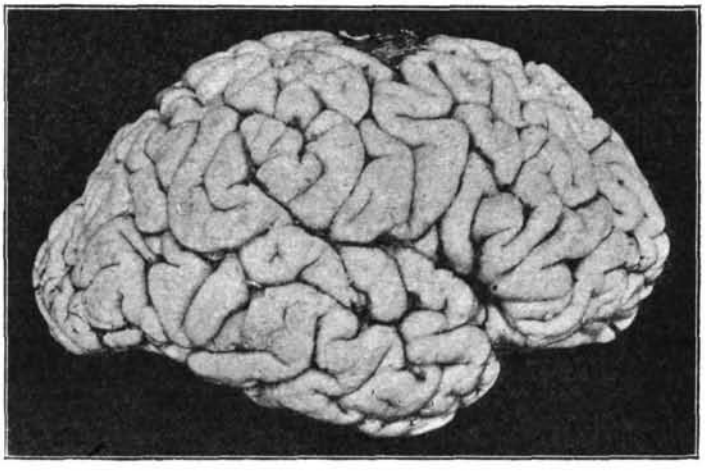

FIG. 64.—Right hemisphere (Case 3).

tore very easily, and when extracted left a small but gaping hole behind. The whole substance of the nucleus in the affected area was greatly shrunken, slightly hollowed out, and clearly in an early stage of definite cavitation. The diameter of the minute punched-out holes averaged 1 to 1½ mm.; the length of the degenerated area was 2¼ cm., and its greatest breadth ¾ cm.

The degenerated area also included the middle third of the external capsule, so that its white fibres no longer stood out clearly between the claustrum and the outer zone of the lenticular nucleus. The claustrum itself appeared normal. The inner zone of the lenticular nucleus (globus pallidus) was certainly somewhat shrunken, but did not look degenerated, while the internal capsule was intact throughout its whole extent. The cortex of the island of Reil looked normal.

Even with the naked eye it was easy to determine that the fine internuncial fibres, so conspicuous a feature of the zones of the lenticular nucleus, had to a large extent disappeared, especially in the area of degeneration. The

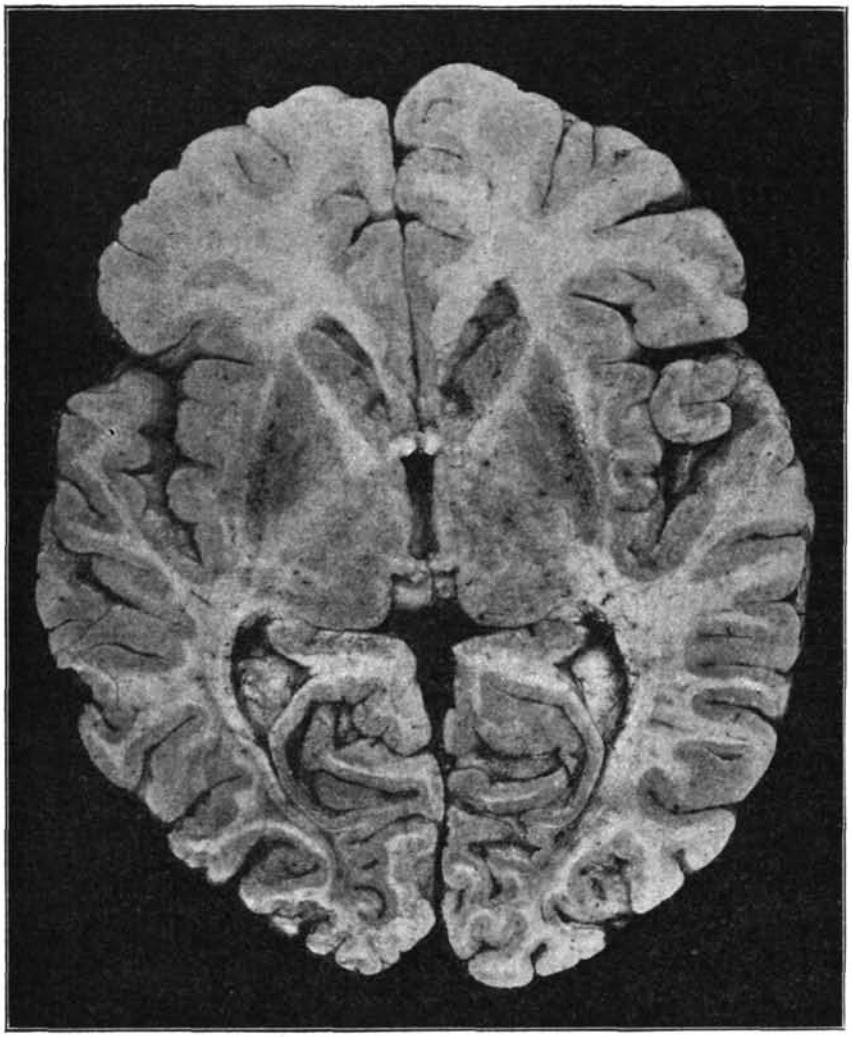

FIG. 65.—*Coupe d'élection* of hemispheres (Case 8). Bilateral symmetrical degeneration and atrophy of lenticular nuclei. Note integrity of internal capsules and normal thalami.

outer lamina could scarcely be distinguished, while the inner lamina, also between the middle and the internal zones, was very indistinct.

There was no other visible abnormality on the transverse section of this hemisphere. The caudate nucleus was possibly in a slightly atrophic state. The optic thalamus appeared perfectly normal.

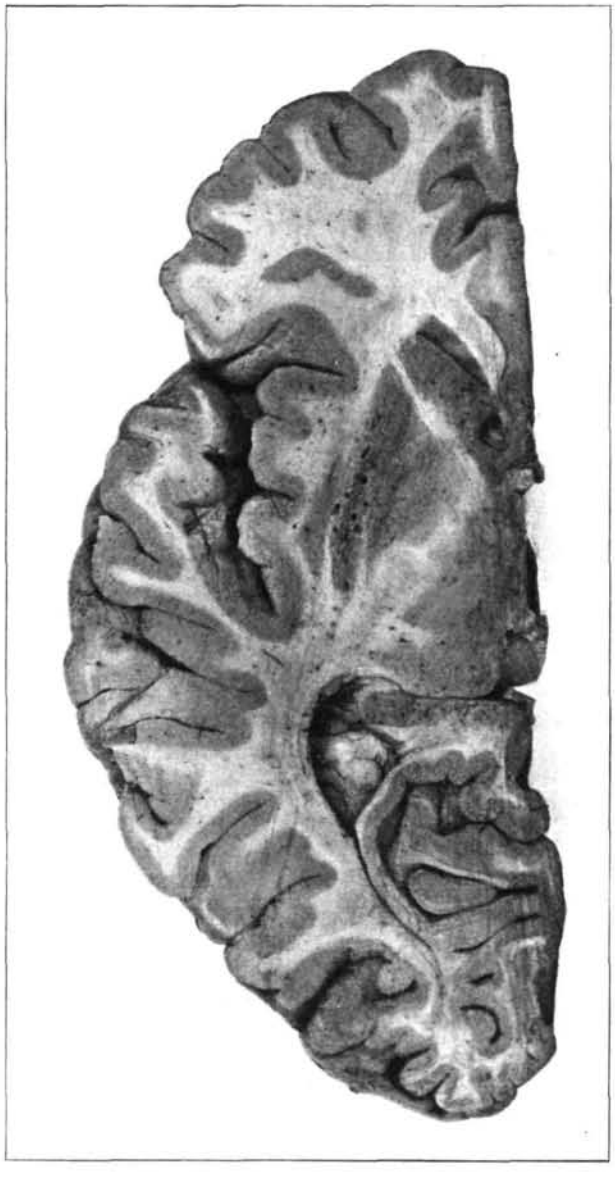

FIG. 66.—*Coupe d'élection*, left hemisphere (Case 3). Atrophic degeneration of lenticular nucleus. Compare in detail with fig. 67.

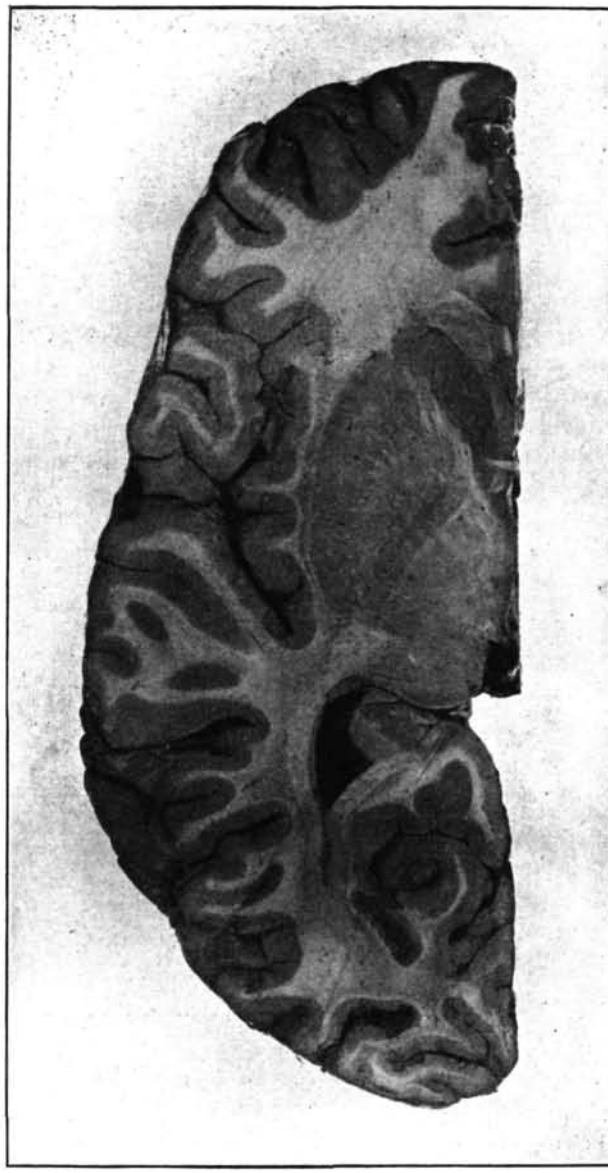

FIG. 67.—*Coupe d'élection.* Normal brain of a youth who died of cirrhosis of the liver without nervous symptoms. Note full rounded contour of lenticular nucleus. Compare in detail with fig. 66.

Left side.—The condition on the left side was remarkably like what obtained on the right, The situation, shape and appearance of the affected area, the slight cavitation, the punched-out little holes, were identical. The affected area presented the same discoloration, felt soft and friable, and was clearly in a state of disintegration. The globus pallidus, in its mesial zone, seemed normal and felt less soft to the touch, but it was somewhat shrunken. There was the same disappearance of internuncial fibres and laminal fibres on the left side, as well as a slight involvement of the middle part of the external capsule. Otherwise there was no change to be noticed. The caudate nucleus and optic thalamus appeared normal; the internal capsule was entirely unaffected.

The affected area on this side had the following dimensions: 2¼ to 2½ cm. long by 1 to 1¼ cm. broad.

There was no hydrocephalus and no ependymitis. Possibly the white matter of the occipital lobes was a little less ample than it ought to have been. The cortex of the frontal convolutions on both sides, the white matter of the frontal lobes, and briefly the whole of the visible cortex, appeared of good depth everywhere.

It is important to compare the naked-eye appearances on this section of the hemispheres of Case 3 with the appearance in the normal brain from a case of cirrhosis of the liver, in a youth, in whom there were no nervous system symptoms.[1]

Fig. 66 represents the left hemisphere of Case 3. The optic thalamus is seen to be as well developed as in the normal brain; the caudate nucleus is perhaps a little small; but the lenticular nucleus is grossly shrunken and atrophic, especially the putamen; its outer contour is no longer rounded and full, but is straighter, in fact, concave at one place; it is darker in colour than in the normal state, is perforated with holes, and has lost its laminal and internuncial striation to a great extent; the external capsule is thinned, and the white matter of the convolutions of the island of Reil looks a little less distinct than it should, although it does not appear to be wasted. The internal capsule (anterior and posterior limbs) is perfectly preserved.

Fig. 67 represents the *coupe d'élection* of the left hemisphere in the case of a boy who died from cirrhosis of the liver, without any nervous symptoms at all. It shows a normal corpus striatum, with a full rounded contour, and the contrast between it and the previous figure is very instructive. The atrophy of the lenticular nucleus in progressive lenticular degeneration becomes in this way strikingly apparent.

[1] For this brain I am greatly indebted to Dr. T. R. Elliott and Dr. Otto May, of University College Hospital.

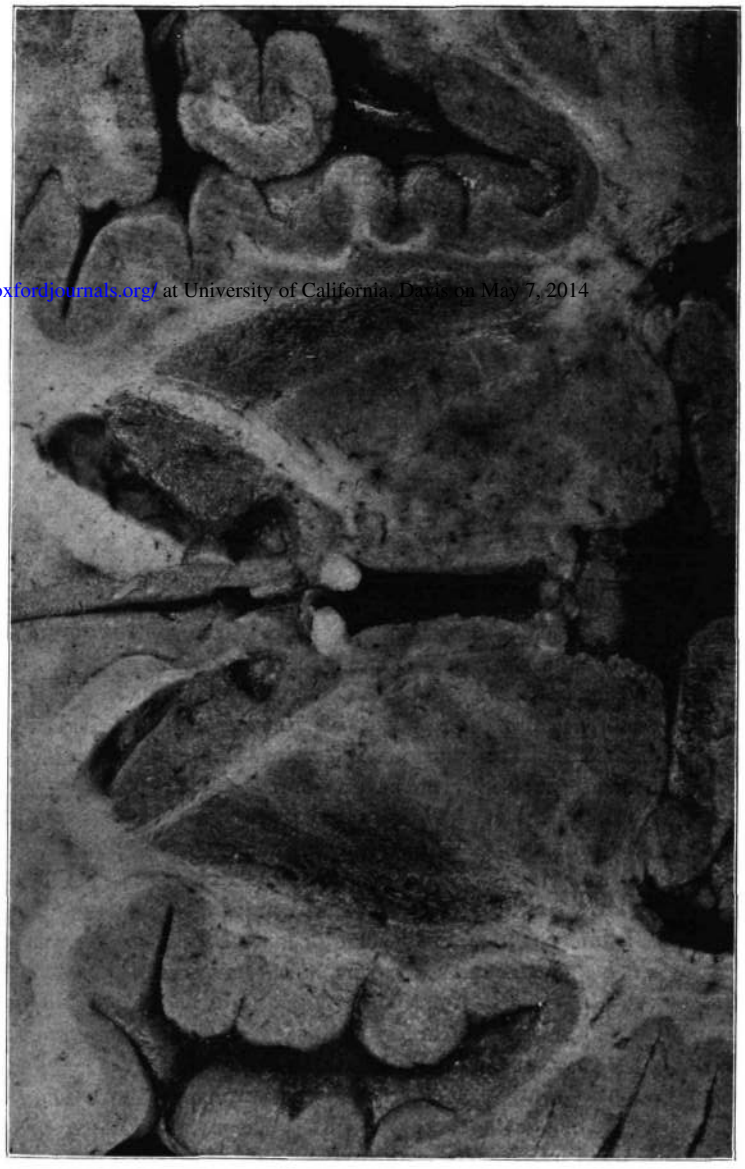

FIG. 68.—*Coupe d'élection*, hemispheres (Case 3). Soft, friable, disintegrated nucleus lenticularis on each side. (About × 2.)

A photograph taken with a higher magnification (fig. 68) shows that the caudate nucleus has retained its fibre-striation in a normal way, whereas the striation of the lenticular nucleus is most defective. It also shows that the globus pallidus is less disintegrated than the putamen, and that the internal capsule and optic thalamus on each side are unaffected to the naked eye.

Microscopical Examination of the Central Nervous System.

On microscopical examination the cord did not present any noteworthy feature. It was of good size on transverse section at various levels, and presented no sign of degeneration. The membranes were not thickened except that the pia-arachnoid looked a little "milky" in one or two places.

(1) *Muscles.*—Sections were embedded and cut in celloidin, and stained by hæmatoxylin-eosin, Van Gieson-Pal's method for intramuscular nerves, counterstained with cochineal.

The chief change was that the muscle-fibres were in many places rounded, instead of being polygonal, and were somewhat separated from each other instead of being closely packed. There was a commencing but still slight interstitial change in many of the sections examined; the muscle-fibres were surrounded by narrow strands of connective tissue with multiplying nuclei. In some places there was increase of nuclei in the sheath of the fibres, but, speaking generally, these changes were nowhere advanced. Many parts of the muscles were indistinguishable from the normal. There were no hypertrophied fibres, and none markedly atrophied. They were all about the same size. The fibres stained well; no alteration in sarcoplasm or myoplasm was discoverable. The muscle-spindles seemed normal. The intramuscular nerves were not obviously changed.

(2) *Peripheral nerves.*—These were not separately examined.

(3) *Spinal cord.*—For the cord the methods utilized were Marchi, Weigert, Weigert-Pal, Nissl, hæmatoxylin-Van Gieson, hæmatoxylin-eosin.

To take the methods for the myelinated fibres first: The sections stained by Marchi's method, from six different levels of the cord, were negative. There was no indication of degeneration, beyond the presence of a few discrete granules, in any of the columns; in particular, the pyramidal tracts, crossed and direct, and the descending anterolateral tracts from the brain-stem, showed no change. Of course, the illness had been of some years' duration, but on the other hand it was essentially progressive, so that the negative result with Marchi is of significance.

The sections stained by Weigert's original method, of which a series is given in figs. 69 to 71, were equally negative. There was no trace of any degeneration in the corticospinal tracts, from the upper to the lower extremity of the cord. The same result was obtained by Pal's method. The columns were all of good size, and stained deeply. There was in some places an indication of a

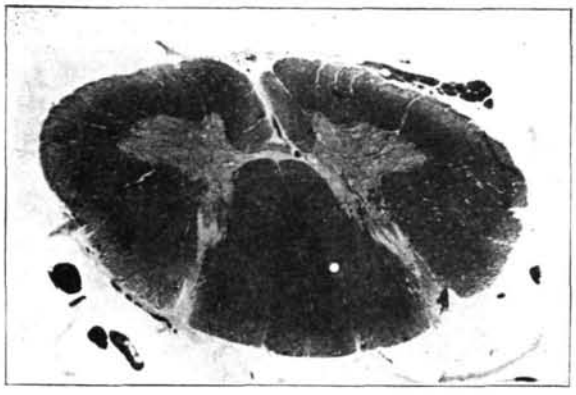

FIG. 69.—Cervical cord (Case 3). Weigert.

FIG. 70.—Dorsal cord (Case 3). Weigert.

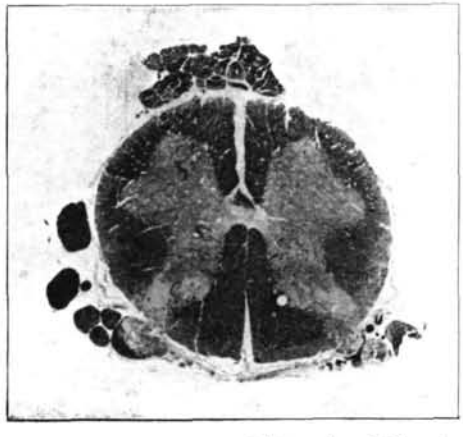

FIG. 71.—Lumbar cord (Case 3). Weigert.

slight peripheral loss of fibres round the margin of the cord, but this was very sparse. The myelinated fibres of the grey matter of the cord stained normally.

With Nissl's method (thionin blue) the anterior horn motor cells were carefully examined at various levels. (Figs. 72, 73.) There was scarcely any loss of cells. In all the sections they were present in good numbers, preserving their ordinary grouping; as a rule they were of good size and shape, and stained well. On the other hand, it was clear that some had undergone a change which is well portrayed in fig. 73. This change is one which is frequently met with in disease of a chronic and progressive nature associated with helplessness and with muscular weakness, for instance, an advancing case of tabes. It consists in a slight shrinkage of the achromatic part of the cell protoplasm, so that the Nissl granules are closely packed together, and the cell, therefore, stains darkly. It is often elongated, and its processes may be less straight than they usually are. But it does not lose its nucleus; the latter remains nucleolated, and it, too, often takes on the stain more deeply. Such cells were often met with in the Nissl sections of the cord. Others showed some pigmentary degeneration: others, again, showed commencing degenerative changes of a less chronic type, in which the tigroid substance becomes more finely granulated, specially round the nucleus, and stains less well, while the nuclear membrane disappears.

Such as they were, the changes may be said to indicate the results of long-continued imperfect use of the musculature, without signifying any definite local atrophic change. Perhaps some of the more acutely altering cells were associated with the effects of a terminal infection.

With ordinary tissue stains it was seen that some leptomeningitis was present, but this was nowhere severe. It was irregularly distributed over the cord, but the significant fact in regard to it was the absence of anything like small-cell infiltration of the meninges. The blood-vessels of the cord, the anterior spinal artery and the intramedullary arterioles, were normal. There was no trace of endarteritis.

(4) *Medulla oblongata and pons.*—The same methods were utilized for these as for the cord.

With Pal's stain for medullated fibres no obvious change could be discovered. The pyramids stained deeply, and were not atrophic in any way; the olives, restiform bodies, fillet, &c., all appeared normal. In the pons there was no change that could be described as pathological.

The sections stained by Marchi's method were not so successful; prolonged immersion of the tissues in formalin militates against good results. No characteristic degenerations, however, were found.

In view of the patient's condition during life the nuclei of the lower cranial nerves were specially examined by Nissl's method. A description of the cells of the hypoglossal nucleus will suffice. If the reader will look at fig. 74 he will see that there is no loss of cells; in other words, the condition is very different from an ordinary bulbar paralysis. The cells stained well and deeply, and the majority were of good shape; others showed the same

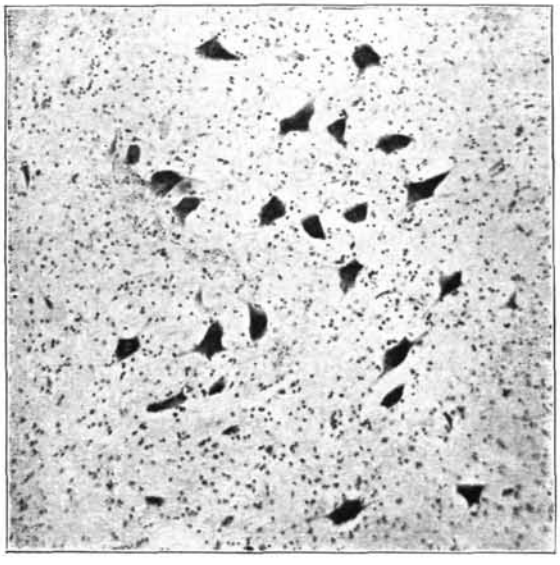

FIG. 72.—Anterior horn-cells, lumbar cord (Case 3). Nissl.

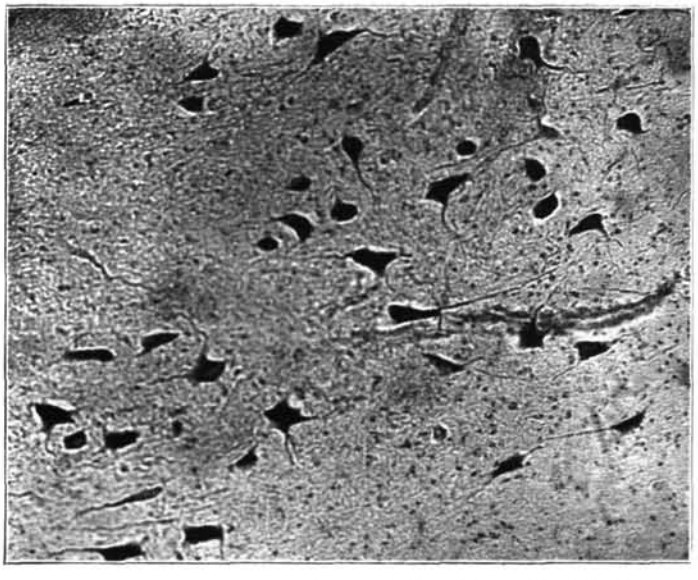

FIG. 73.—Anterior horn-cells, cervical cord (Case 3). Nissl.

elongated and "intensified" appearance that has been already noted in the spinal cord.

The cells of the facial and other motor nuclei were similarly numerous, not atrophic, and many showed the changes that have just been described. Round a few of the nuclear cells parasite glial cells were found.

(5) *Cerebellum.*—The cells and fibres of this organ seemed quite normal with the same stains as for the cord. The Purkinje-cells, granular layer, dentate and other nuclei, presented no departure from similar sections of a normal case used as a control.

(6) *Crus.*—Weigert and Weigert-Pal sections of the crus cerebri (fig. 75)

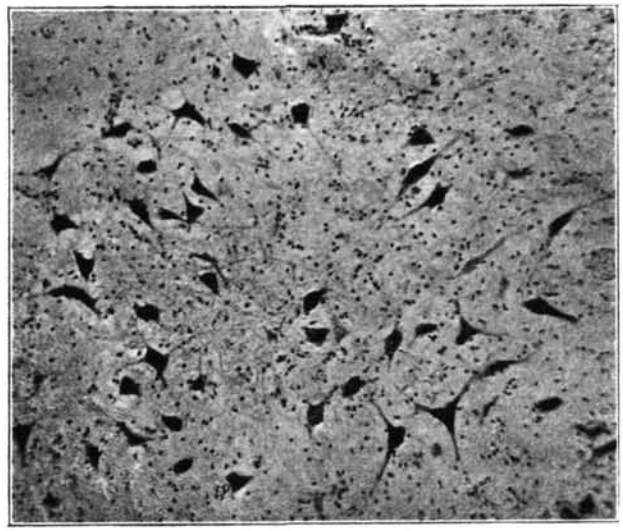

FIG. 74.—Right hypoglossal nucleus (Case 8). Nissl. Notice that there is no loss of cells.

were in every respect normal. The pyramidal fibres were apparently intact, stained well, and were not diminished in quantity, compared with similar sections from a normal brain. The components of the crus on either side of the pyramidal tract were unaffected. The substantia nigra was not obviously altered. The tegmentum was not deficient in any way. The fibre-content of the nucleus ruber seemed normal.

With Nissl's method the cells of the nucleus ruber were examined. They were not diminished in number; most of them stained well, and were of normal shape. Not a few stained rather poorly, while still preserving their shape. Round many of them were parasite neuroglial cells in considerable numbers (fig. 76)—a condition which is almost certainly indicative of failing nutrition of the nerve-cells, from excessive functionary, or from other causes.

(7) *Basal ganglia, internal capsule, and subthalamic region.*—On the right side the central part of the hemisphere was cut into slabs by a series

FIG. 75.—Crus cerebri (Case 3). Weigert. Normal appearance.

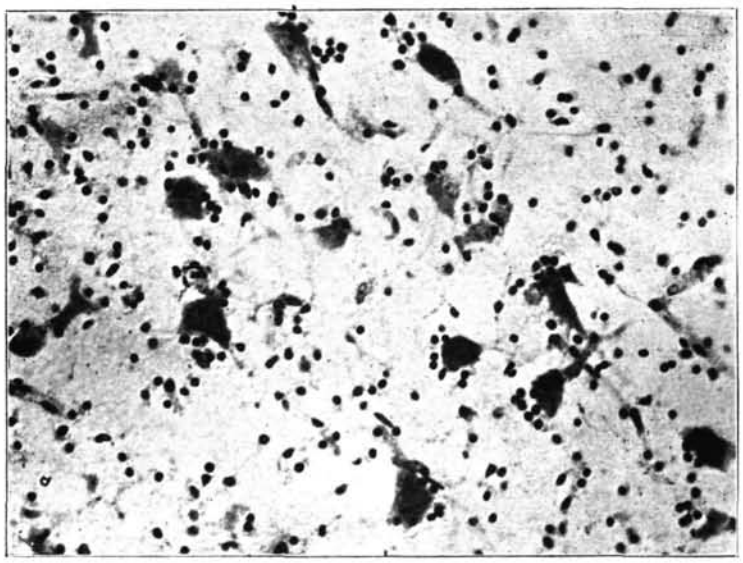

FIG. 76.—Cells of red nucleus (Case 3). Nissl. Numbers of parasite glial cells round many of the nerve-cells.

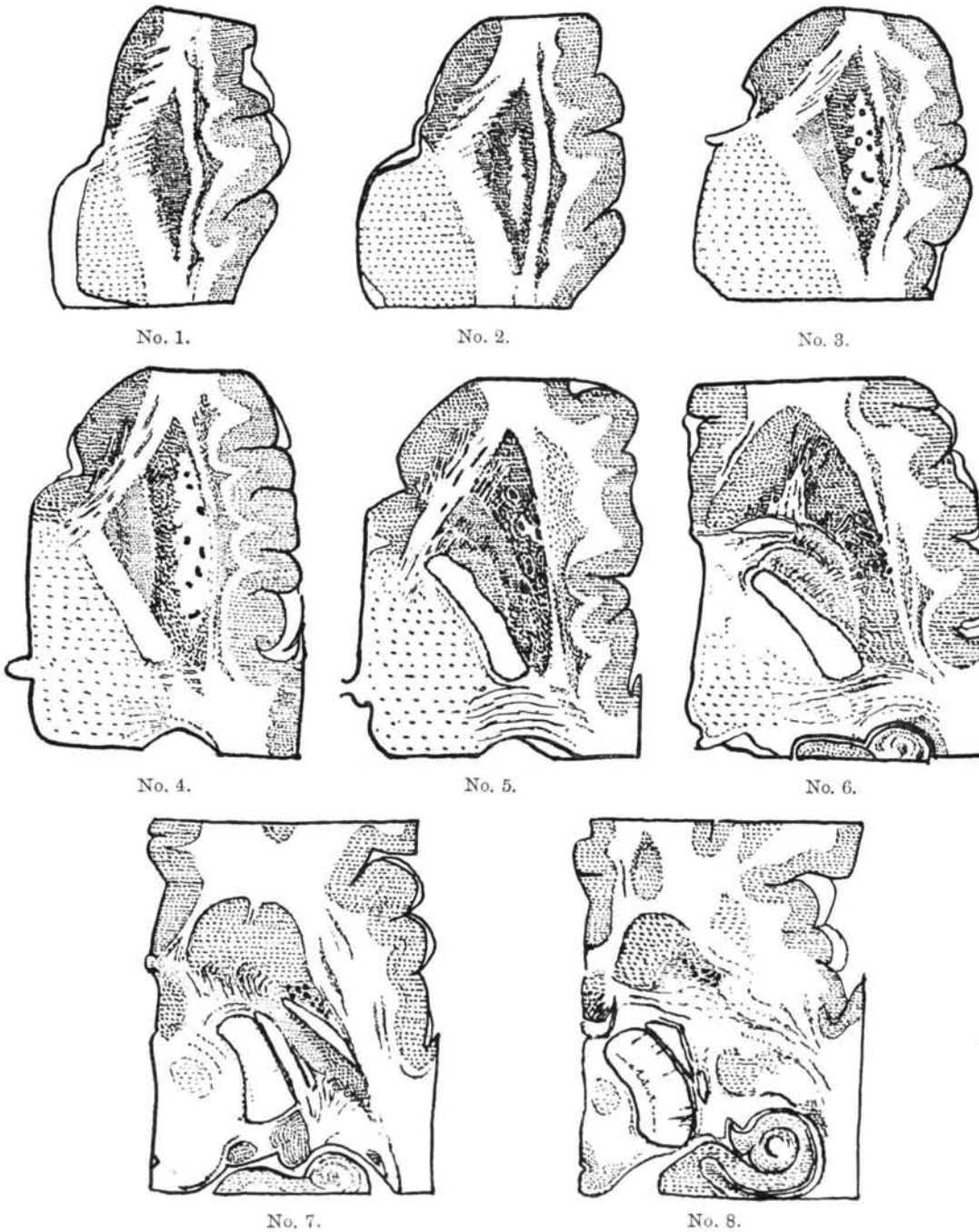

FIG. 77.—Drawings of cut slabs of right basal ganglia (Case 3). Natural size. For description see text.

of incisions exactly parallel to the *coupe d'élection*. Some of these were taken for Nissl and ordinary tissue stains, others were placed in Müller's solution for Pal and Weigert. On the left side similar slabs were cut; some were utilized for Marchi, others for a Weigert-Pal series of the subthalamic region.

(*a*) *Minute anatomy of the lenticular degeneration.*—The accompanying series of drawings represents the appearance of the upper aspect of the cut slabs of the right hemisphere, from above downwards, and serves to give, as it were, a reconstruction of the lenticular degeneration.

No. 1 represents the putamen above the level of any visible degeneration, with a normal internal and external capsule, claustrum, &c. In No. 2 the area of disease has made its appearance, and is seen to occupy a somewhat crescent-shaped strip of the putamen, towards its outer side, while the beginning of the middle zone (globus pallidus) just appears to its inner side. The external capsule appears intact. In No. 3 the affected area is broader, occupies posteriorly almost the whole breadth of the putamen, touches the external capsule slightly, and contains in its centre the gaping holes round the lenticulo-striate vessels that have already been mentioned. No. 4 shows the appearance at the *coupe d'élection*, and corresponds to the photograph reproduced as fig. 65. No. 5, a little lower, still shows clearly how the degeneration is related to the lenticulo-striate vessels; it appears to be confined at this level to the putamen. The globus pallidus appears unaffected, at least directly. Further down, through Nos. 6, 7, and 8, there is no degeneration to be seen by the naked eye, and where the lenticulo-striate vessels enter the brain they appear to be normal, nor is there any recognizable area of softening round them.

In the sections stained with hæmatoxylin-eosin, under a low power, there was found a broad strip, occupying almost the whole of the putamen, which stood out prominently and unmistakeably. Here there was a pronounced degree of sclerotic change, consisting in a great overgrowth of neuroglia, which in a number of places was commencing to break down. The internuncial fibres from the putamen could not be distinguished; the nerve-cells of the nucleus were few and far between. In and round this area the blood-vessels were somewhat dilated, with widening of the space of Virchow-Robin around them, occasioned probably by retraction of the tissues under the action of sclerosis. Towards the periphery of the degenerated area the sclerosis was densest, towards its centre it was thinner, and there the tissue was commencing to break down; no doubt more cavitation would have ensued had the patient lived longer. Fig. 78 gives an idea of this low-power appearance.

With a higher magnification this whole area was seen to be a confused mass of neuroglial overgrowth and tortuous small vessels, forming an amorphous network in which the true nerve-elements of the nucleus were lost. Fig. 80 gives an excellent impression of the density of this change in the putamen, and illustrates well the amorphous character of the degeneration.

Under a still higher magnification (fig. 81) it was noted that the nerve-cells of the putamen had almost entirely disappeared; only a few could be discovered.

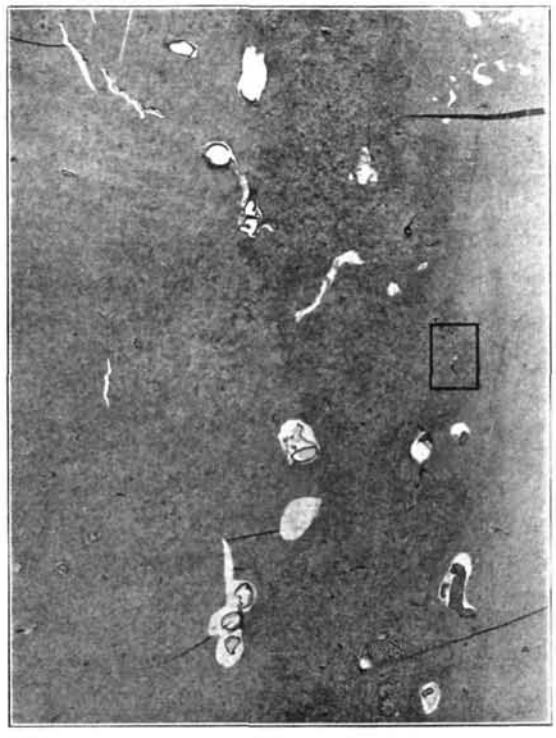

FIG. 78.—Degenerated area of right putamen (Case 8). For key see fig. 79. [ ] = fig. 80.

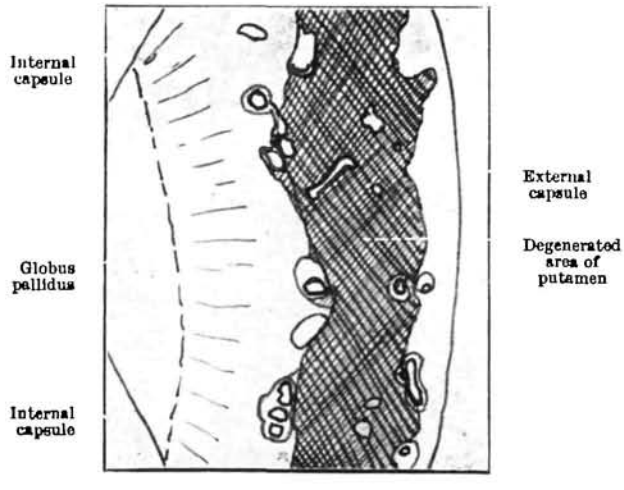

FIG. 79.—Key to fig. 78.

Neuroglial nuclei and cells and fibres formed the chief feature in the picture. In some places they were actively growing; in others they were sparse, where the tissue was breaking down. Everywhere numbers of the so-called "Körnchenzellen" could be seen. Such nerve-cells of the putamen as were left were usually shrunken and stained very deeply. With Marchi's method some of the few nerve-cells that remained were found to be full of minute fat-granules. The bundles of internuncial fibres leaving the putamen to enter the globus pallidus were very difficult to trace.

The condition of the blood-vessels deserves special attention. As has already been remarked, under a low power, so far from being thickened or obliterated, they were if anything thinned and dilated. The wide spaces

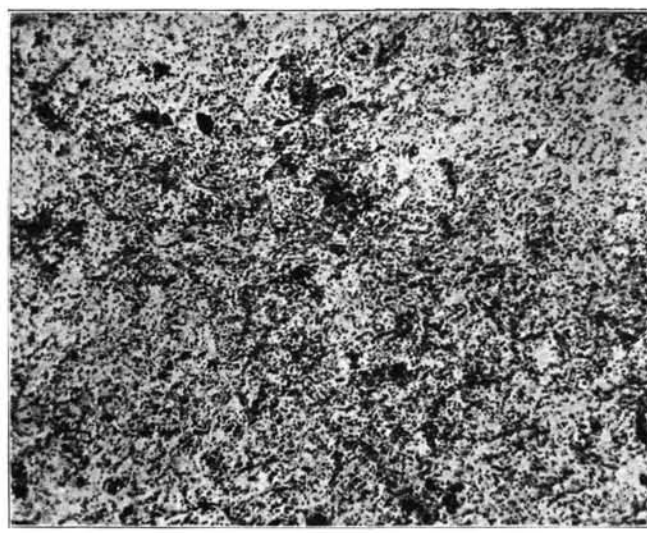

FIG. 80.—Degenerated area, right putamen (Case 3). Hæmatoxylin-eosin. A mass of amorphous neuroglial overgrowth, breaking down in some places. (× 60.)

surrounding them were mostly empty; the margins were formed of a feltwork of neuroglia. Towards the centre of the diseased area, however, the same spacing was not remarked, and there was a considerable degree of disintegration round the vessels. Under a higher power there was no trace of any small-cell infiltration that would suggest an inflammatory reaction. The lymphatic sheaths of the vessels were somewhat dilated, but they did not contain small round cells. The coats of the lenticulo-striate arteries could be seen to be of normal proportions; in no single vessel was there any end-arteritis; the elastic lamina was mostly intact, the muscular layer was a little thinned or stretched, the adventitia was in some instances perhaps a little thickened. The arterioles and capillaries, also, were free from any sign of

endarteritis. In scores of sections I failed to discover a single obliterated vessel. (Fig. 82.)

Compared with the putamen, the cells of the globus pallidus were less interfered with, though still much diminished; this section of the nucleus lenticularis showed little change (with hæmatoxylin-eosin), beyond increase in neuroglial nuclei and a general increase in the density of its tissues. Similarly the cells of the claustrum revealed little, if any, pathological change, and its neuroglial groundwork was practically normal.

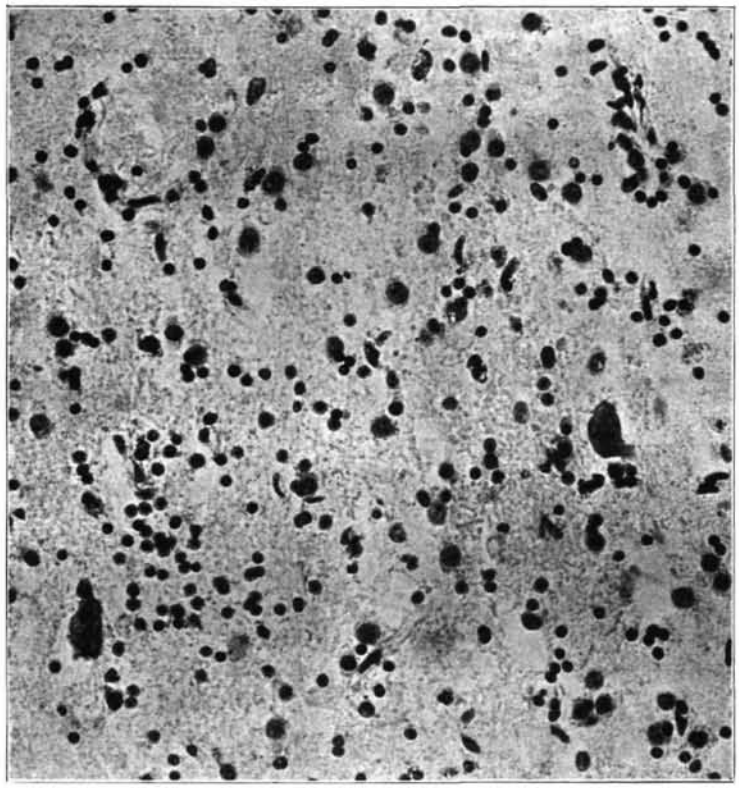

FIG. 81.—Degenerated area, right putamen (Case 3). Nissl. (× 500.) Two degenerated nerve-cells, neuroglial cells, "Körnchenzellen," &c. Tissue breaking down.

Sections from the degenerated portion of the lenticular nucleus, stained with osmic acid, showed the presence of great numbers of large round phagocytic cells crammed full with fatty granular débris, but only where the tissues were actually disintegrating. Round the edges, where the neuroglial overgrowth was densest, these cells were not found. (Fig. 83.)

(*b*) *Optic thalamus and caudate nucleus.*—No changes in these ganglia, analogous to what obtained in the putamen, could be found. The cells of the

different nuclei of the thalamus (anterior, external, ventral) were for all practical purposes normal, and similarly with the cells of the caudate. There were no neuroglial changes that could be distinguished with certainty.

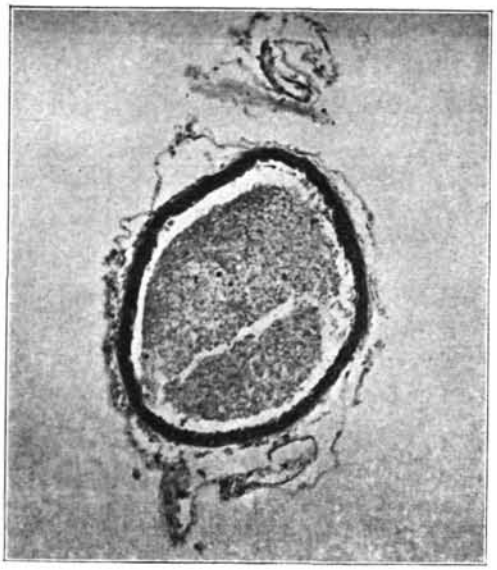

FIG. 82.—A single minute lenticulo-striate vessel, removed and cut separately (Case 3). Hæmatoxylin-Van Gieson. It is, if anything, thinned. No trace of endarteritis.

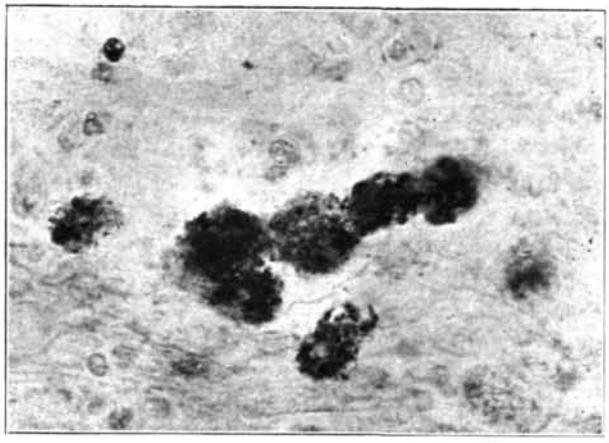

FIG. 83.—Macrophages from the degenerating area, left lenticular nucleus (Case 3). Marchi. They are crammed with fatty granular débris.

(*c*) *Internal capsule and fibres of the corpus striatum.*—By the methods of Weigert and of Weigert-Pal the fibre-content of the basal ganglia was investigated.

In a series of sections cut consecutively from above downwards it was seen that the maximum of defect was in the middle third of the putamen, regarded vertically, and to a less extent in the upper third; in the lower third, however, there was also a profound fibre-defect.

In a section at the level of the upper part of the corpus striatum the internal capsule was perfectly normal, and the pencils of fine fibres passing from the putamen mesially were also normal. A little lower, at the level of the upper margin of the globus pallidus (fig. 84), disintegration commenced

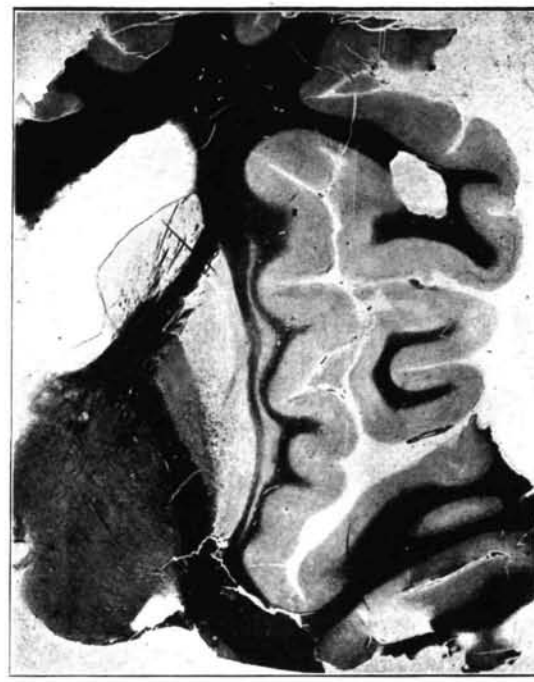

FIG. 84.—Horizontal section, right hemisphere (Case 8). Weigert. Note integrity of internal capsule and optic thalamus, normal fibre-content of caudate, atrophic degeneration of putamen, and of globus pallidus (to a less extent). Note also slightly imperfect external capsule.

in the putamen, in its middle third. There, the pencils of internuncial fibres were atrophic, and many had disappeared; at the anterior and posterior extremities of the nucleus, however, they were still in evidence. The outer margin of the putamen, instead of being rounded, was in two places concave, indicating considerable loss of substance. The external capsule at these two places was itself thinned, and took the stain feebly. At the level of the middle of the globus pallidus, regarded vertically, there was much atrophic change in the putamen, both as regards its size and its fibres. The external lamina was very incomplete. The external capsule was defective, as noted

already. The inner lamina was also defective and the fibres passing from the middle to the inner segment of the lenticular nucleus, though present in fair numbers, stained much less well than normally. The fine fibres coming across the anterior limb of the internal capsule, from the caudate to the putamen, stained well, and did not appear obviously reduced in numbers. The internal capsule was unaffected throughout. The fibres underlying the convolutions of the island of Reil were not involved.

FIG. 85.—Horizontal section, right hemisphere (Case 3). Weigert. Grossly atrophic putamen and globus pallidus. Compare in detail with a corresponding section from a normal brain (fig. 86).

At a still lower level (fig. 85) the atrophy of the shrunken putamen was very apparent. It was riddled by small holes, some of which were confluent, notably along the outer margin of the nucleus. Its fine fibres were almost all diseased. The laminæ of the nucleus were greatly degenerated, and in

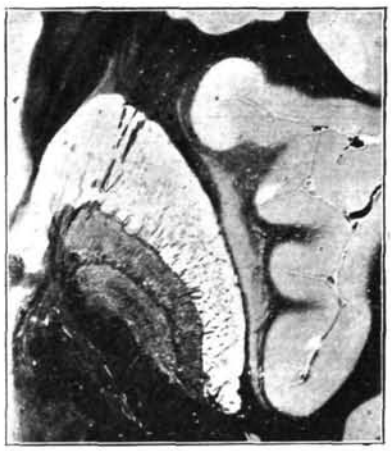

FIG. 86.—Section of normal brain corresponding to that of fig. 85, Weigert. Note in particular the normally staining globus pallidus and laminal and internuncial fibres.

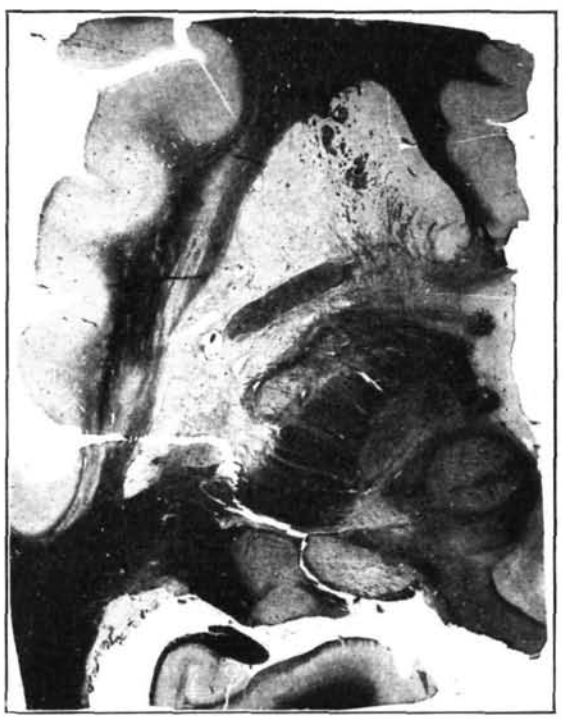

FIG 87.—Subthalamic region, left hemisphere (Case 3). Weigert. (About $\frac{2}{3}$.) Description in text.

particular the fine fibres of the globus pallidus were affected to such an extent that they could scarcely be traced. If the appearance in this figure is compared with that of a normal brain taken at the same level, the contrast between the healthy and the degenerated globus pallidus is very noticeable (fig. 86). The external capsule was as described above.

In the subthalamic region (figs. 87 and 88) it could be seen that the ansa lenticularis, where it sweeps round the crus, was partly affected; it did not stain so deeply as some of the neighbouring structures, nevertheless it still contained a number of apparently healthy fibres. The strio-Luysian fibres could be readily distinguished; many were degenerated, but probably an equal number seemed normal. No doubt, some at least of these were passing in the reverse

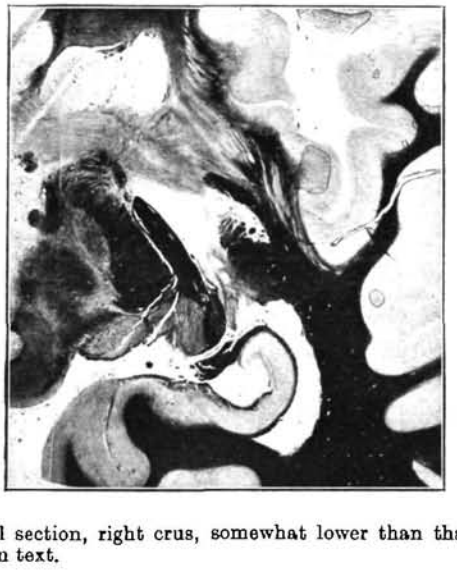

FIG. 88.—Horizontal section, right crus, somewhat lower than that of fig. 87 (Case 3). Weigert. Description in text.

direction. The prolongation of the ansa lenticularis to the capsule of the red nucleus (Dejerine) could not be followed satisfactorily. The lenticular bundle of Forel was slightly degenerated. The corpus Luysii was somewhat smaller than normal, and on the whole its fibres stained rather less well than usually; nevertheless, on microscopical examination only relatively few diseased fibres could be found in it. The zona incerta did not appear obviously altered, except that perhaps it was a little smaller than in sections from a control brain. The field of Forel stained normally. Further back, its place is taken by the red nucleus, which in the present case was not apparently defective in any way.

The fibres in the external segment of the optic thalamus, and those crossing the capsule from the corpus striatum to that part of the thalamus, were slightly reduced in numbers, but most of them took the stain deeply. The

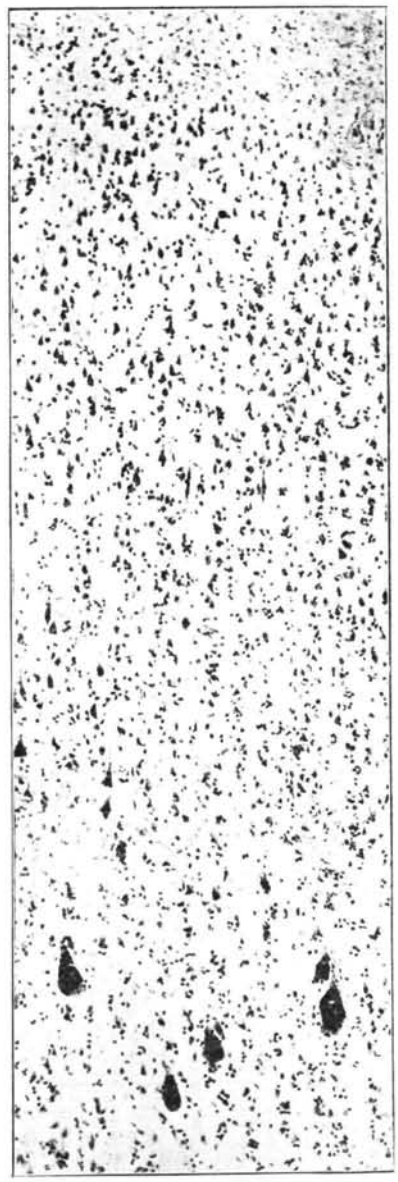

FIG. 89.—Strip from precentral gyrus, left leg centre (Case 3). Nissl. Normal Betz-cells.

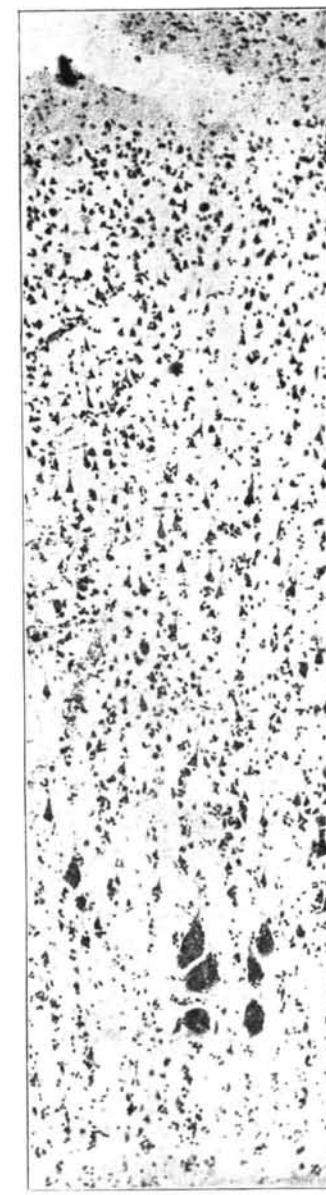

FIG. 90.—Strip from precentral gyrus left arm centre (Case 3). Nissl. Normal Betz-cells.

"zone grillagée" and the external medullary lamina of the thalamus were not altered to any great extent.

The whole of the subthalamic region on the left side was cut in serial section by Marchi's method, but no positive change was discovered except that the ansa was definitely though not profoundly degenerated. The staining, however, owing no doubt to the tissues having been in formalin so long, was not perfect.

(8) *Cortex cerebri.*—The left motor area was investigated by a series of pieces taken from it, to include both the precentral and the postcentral convolutions. In addition, the cortex of the island of Reil, as well as of the posterior and of the third left frontal convolution, was examined. Special attention was given to that part of the motor area, at the lower end of the precentral gyrus (operculum), from which originate the fibres that innervate the muscles of articulation, viâ the bulbar nuclei.

Figs. 89 and 90 represent strips of the cortex of the leg and of the arm area. There was, in the first place, no defect in number, or in shape and staining properties, of the Betz-cells. Further, the zonal layer, outer granular layer, pyramidal layer, Betz-cell layer, and fusiform layer, could be readily distinguished, and were not obviously defective in any way. Some of the pyramidal cells showed small collections of glia-cells round them, and possibly they were slightly diminished in number.

In the other portions of the cortex examined there was little or no departure from the normal. In particular, the motor centre for articulation showed no obvious loss of cells, although here the pyramidal cells seemed in some instances to be unduly elongated and to stain too deeply.

In no one of many scores of sections was there any trace of small-cell infiltration of cortical vessels.

The fine myelinated fibres of the motor cortex were examined by the method of Pal. There was some diminution in the fibres of the tangential layer, or zonal layer. It was not so dense and well defined as in the normal brain. On the other hand, the supraradiary and intraradiary networks were apparently unaltered.

Microscopical Examination of other Organs.

(i) *Liver.*—The histological methods employed were hæmatoxylin-eosin, hæmatoxylin-Van Gieson, Weigert's stain for elastic tissue, Sudan III for fat.

The liver presented a very interesting appearance under a low magnification. Its substance was divided into numerous islets of highly irregular size, most of them including perhaps six or eight lobules, or liver units. Others were so small as to include only one lobule—of these only a few were seen—and in other instances less than one lobule, in fact only a few liver-cells were enclosed in cirrhotic tissue. This fact was determined by the use of serial sections. Speaking generally, the cirrhosis was of mixed but mainly multilobular type. Round the islets was cirrhotic tissue in abundance, of varying breadth, much

more cellular than fibrous, on the whole, and containing numerous young connective tissue corpuscles. A very prominent feature of the cirrhotic strands was the presence of so-called hypertrophying bile-ducts. In some places these were almost the only structures that could be seen in the field. There was little sign of intralobular cirrhosis; in a few places strands of connective tissue appeared to be dividing up the columns of liver-cells, but there was so little of this change as to be negligible.

The curious feature of the cirrhosis was its pronounced irregularity as far as its effects on the liver-cells were concerned. While many lobules were

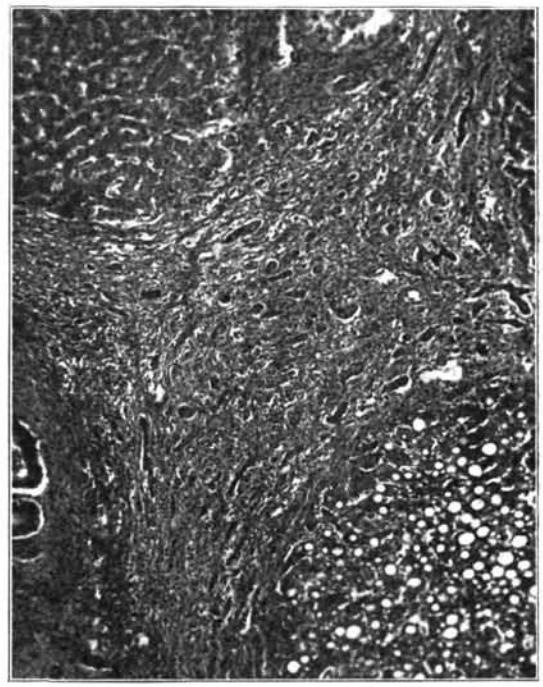

FIG. 91.—Liver (Case 3). Hæmatoxylin-eosin. Healthy and degenerated liver-tissue.

normal, others in their neighbourhood were not merely irregularly degenerating, but were sometimes in a state of what appeared to be acute necrosis. The whole of the centre of the lobule would be seen to be losing its cellular structure, and to be staining homogeneously, indicative of some acute chemical change. The liver-cells were in many places normal in every way; others in the same lobule might be in a state of advanced fatty degeneration. Stained with Sudan III the picture obtained was striking. Some nodules of cirrhotic tissue contained only fat-cells, so to speak; others contained no fat at all.

Abundant evidence was obtained, under a high power, of active regeneration of liver-cells. In the regenerating area it was often observed that the nuclei

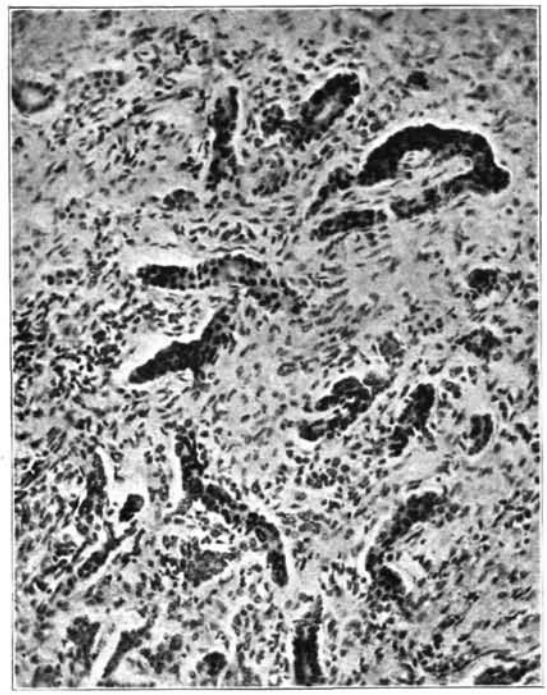

FIG. 92.—So-called hypertrophying bile-ducts in cirrhotic tissue of liver (Case 3). Hæmatoxylin-eosin.

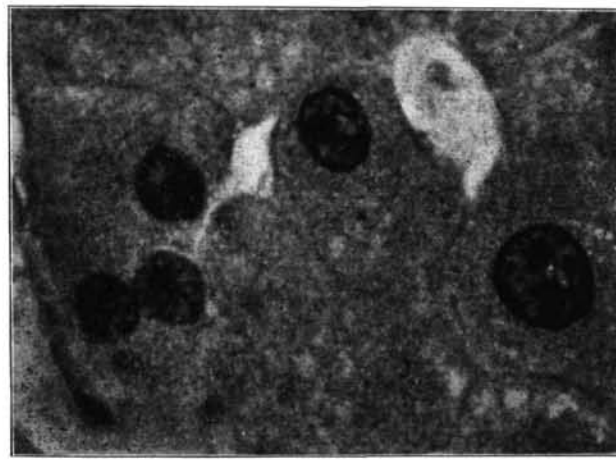

FIG. 93.—Regenerating liver-cells (Case 3). Division of nuclei. Hæmatoxylin-eosin. (× 1,200.)

stained irregularly with polychrome blue, some being pinkish, others bluish; sometimes the nucleus was blue with a bright red nucleolus. Here were to be found cells undergoing amitotic division, in most instances, although a rare mitotic figure was here and there seen. Many cells had double nuclei, others hypertrophying nuclei. These varying appearances are shown in the accompanying figures (figs. 91 to 94).

One of these is instructive (fig. 94), as it shows direct continuity of the hypertrophying bile-ducts with columns of liver-cells. The portal tracts and vessels of the liver did not present any marked abnormality.

Another feature seen in the liver sections will be noted subsequently.

(ii) The other organs examined microscopically must be briefly dismissed.

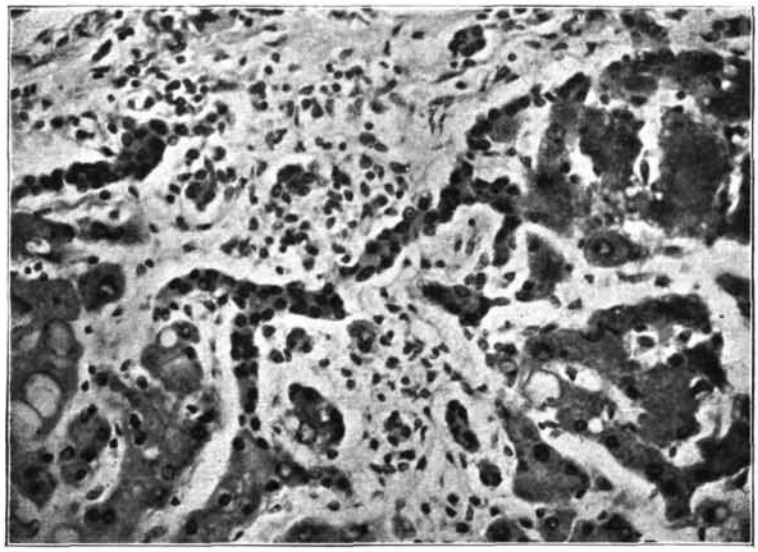

FIG. 94.—Continuity of so-called hypertrophying bile-ducts with columns of liver-cells (Case 3). Hæmatoxylin-eosin.

The thyroid showed changes such as are reproduced in fig. 95. The colloid vesicles were in many places reduced in size and number, and contained less colloid than in the normal gland. The epithelium lining the vesicles was often noticed to be in a state of proliferation. A certain amount of interstitial change was present.

The suprarenal gland did not present any unusual feature.

The thymus was of course small, but some of its tissue was persistent; it appeared to be normal.

The spleen, on microscopical examination, showed little change; what change there was indicated interstitial alteration.

The kidney did not present any unusual feature.

The pituitary also showed no obvious pathological change.

(iii) The sole remaining point in the pathology of this case of progressive lenticular degeneration is the question of a terminal infection. Scattered through the suprarenal gland, to a very much less extent in the liver, but also

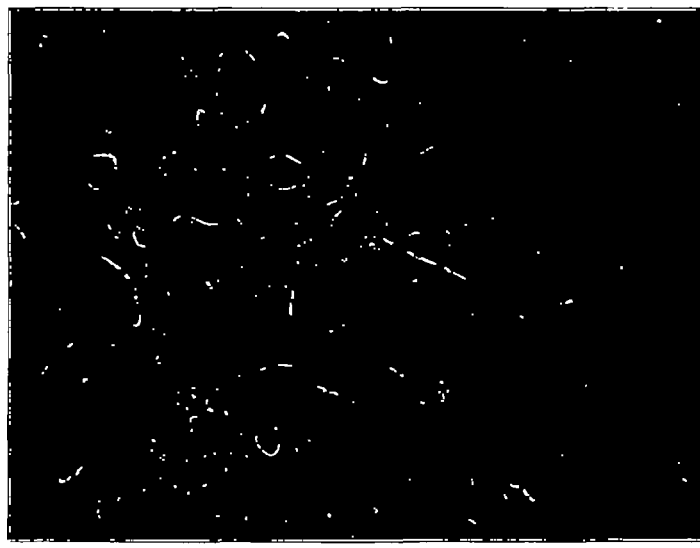

FIG. 95.—Thyroid (Case 3). Hæmatoxylin-Van Gieson.

FIG. 96.—A minute vessel removed from degenerating lenticular area and cut separately (Case 3). Shows a plug of bacilli entangled in a fibrin clot. Hæmatoxylin-eosin.

in the brain, cord, and kidney, clumps of bacilli were here and there to be found. Fig. 96 is specially interesting, for it represents a transverse section of a minute vessel from the degenerated area in the lenticular nucleus. Entangled in the fibrin clot will be seen a mass of bacilli, stained intensely

blue-black. In view of the scattered nature of the process it is, I think, probable that its sole significance is that of a terminal infection, possibly from the alimentary canal. The bacilli resembled the *Bacillus coli* structurally, but their staining reactions seemed in one or two ways to be rather different.

Résumé of the Pathological Findings in Case 3.

The brain is of good size and shape, and its convolutional pattern is normal. There is no obvious atrophy of gyri, and no definite disease of the membranes, beyond slight irregular "milkiness" of the arachnoid in the interpeduncular space and on the posterior aspect of the cord. The pons looks perhaps a little small in proportion.

The cerebral blood-vessels are not thickened and show no patches of disease in their walls. They are all patent.

The brain is cut open by Marie's *coupe d'élection* and at once a bilateral and strikingly symmetrical degeneration of the lenticular nucleus, in particular the putamen, meets the eye. This structure is seen to be grossly shrunken, so that its outer margin is irregularly concave, instead of being rounded and convex; it is darker in colour than normal, looks friable and feels soft, is so disintegrated that a cavity formation has begun, and is perforated by small gaping holes, in some of which the lenticulo-striate vessels, separated from the surrounding tissue, can be seen. The dimensions of the degenerated area average 3 by 1 cm. Compared with a normal brain, the lenticular nucleus is in this case considerably shorter and narrower, indicating the extent of its atrophy. The globus pallidus is less affected; the laminæ and internuncial fibres between the zones of the nucleus have disappeared to a great extent in the outer section; on the inner side they are better preserved; lower down, however, the globus pallidus has undergone a great loss of fine fibres. The caudate nucleus is a little shrunken, but the optic thalamus is normal, and the internal capsule is entirely untouched.

The softened portion of the lenticular nucleus occupies approximately the middle third of the putamen, vertically considered; in the lower third there is still much shrinkage, but on the whole less disintegration. Microscopically the putamen is found to be extensively sclerosed by neuroglial overgrowth, which is breaking down in the centre; the normal cells of the nucleus have to a great extent disappeared, and numerous "Körnchenzellen" are present; macrophages abound in the degenerate area; but there is no small-cell infiltration

to indicate an inflammatory reaction, and no sign of endarteritis in the vessels of the affected region.

Although the cortex and subjacent structures of the island of Reil have the same vascular supply, they are not involved, with the exception of the middle third of the external capsule, which is thinned, and its posterior third, which is degenerated.

The cortex in the motor area, from the cyto- and myelo-architectonic points of view, is found to be normal. The pyramidal system, from the Betz-cells, through internal capsule, crus, pons, medulla, cord, anterior horn-cells, to the muscles, is exhaustively examined, but no alterations of any significance are found at all, except such as can be accounted for by the helpless and emaciated condition of the patient.

There is some degeneration in the extrapyramidal system from the lenticular nucleus viâ the ansa lenticularis towards the red nucleus, but the cells of the latter structure are mostly normal. Many strio-Luysian fibres are degenerated; others (some of which may be passing in a reverse direction) are normal. The corpus Luysii is rather small, and somewhat degenerated. Most of its fibres, however, stain well enough. The lenticular bundle of Forel is slightly degenerated. There is little change in the external medullary lamina of the optic thalamus, or in the "zone grillagée"; on the whole the fibres of the thalamus are well preserved.

The liver is found to be in an advanced state of cirrhosis, typically multilobular, but to some extent mixed; there is apparent increase of bile-ducts in the cirrhotic tissue, great variations in the condition of the liver-cells, many being in a condition of fatty degeneration, others normal, and others still actively regenerating, amitotic and less frequently mitotic division being seen in the last.

The spleen is slightly enlarged, but otherwise normal.

The thyroid shows interstitial changes chiefly, but there is also proliferation of epithelium.

The pituitary, thymus, and suprarenal do not present any special abnormality.

There are indications of a terminal infection in the presence of clumps of bacilli in some of the internal organs, as well as in the brain and cord.

Case 4.—The patient whose case is No. 4 is still living (December, 1911).

Case 5.—In Case 5 there was no pathological examination.

Case 6.—The autopsy was made on February 15, 1889, and is described in the notes as follows:—

"The brain-tissue was soft, probably œdematous.

"The membranes were healthy. On naked-eye examination no obvious morbid appearance could be made out.

"The spinal cord was firm; the membranes not adherent.

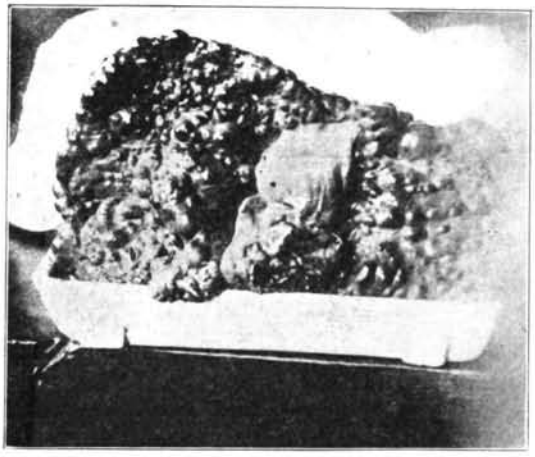

FIG. 97.—Naked-eye appearance of liver (Case 6, National Hospital, 1889).

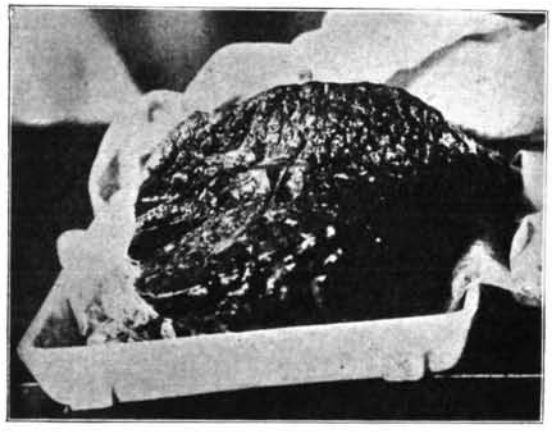

FIG. 93.—Transverse section of liver (Case 6).

"The liver was small, contracted. Small nodules, varying in size, many about the size of a small marble, all over surface. Section corresponds. Extreme cirrhosis of liver.

"Spleen large, fairly firm, much congested."

There is no record of any further examination, or of any microscopical investigation.

The appearance of the liver is reproduced as figs. 97 and 98, from the original negatives kindly lent to me by Dr. James Taylor.

Chapter IV.—Synthetic Study of the Disease.

For the purposes of a synthetic study of progressive lenticular degeneration we have now at our disposal eleven cases, or, with the inclusion of two less certain cases, thirteen in all. Of these two, since Anton's is more doubtful than the other (my own Case 6) it will be excluded, so that this study is based on twelve recorded cases, in no fewer than ten of which an autopsy was held. Clinically and pathologically, therefore, there is abundant material for a systematized description of the disease. Of these twelve cases, six date back more than twenty years, the other six are reported in this paper for the first time.

(1) Definition and Terminology.

"Progressive lenticular degeneration" is the nosological term with which I propose to denote the disease. Of the other terms which have been proposed, that devised by Gowers is the only one, in my opinion, which has any claim to recognition. The disadvantages of "tetanoid chorea," however, outweigh its advantages. Although pathology, where possible, should be called on to supply the name for a disease in preference to clinical medicine, the term was coined at a time when the pathology of the disease was obscure. Further, "tetanoid chorea," considered clinically, may be misleading. In the large majority of the recorded cases the involuntary movements, which form a prominent clinical symptom, are of the nature of tremor rather than chorea; moreover, "tetanoid" is not sufficiently distinctive. Anton proposed the term "dementia choreo-asthenica" to characterize his case, which is a case of congenital cerebral syphilis, but the title is for other reasons unsuitable. From the point of view of the most definite cases, to include "dementia" in the title gives that symptom undue prominence, even admitting that dementia is the correct term to employ. Objection, too, may be taken to the use of the epithet "asthenica." The asthenia of progressive lenticular degeneration is very different from that of neurasthenia or of Addison's disease.

It seems to me that "progressive lenticular degeneration" is a descriptive term which is brief, distinctive, based on pathological data, and at the same time non-committal, inasmuch as it entails no acceptance of a particular hypothesis as to the actual nature of the disease.

In view of the fact that the clinical symptoms are exclusively nervous, it is well to adopt a neurologically descriptive term. The essential fact of the hepatic cirrhosis may be mentioned in a sub-title. What I have done is to select what is by far the most striking pathological feature of the disease from the nervous standpoint and to utilize it for purposes of nomenclature, and, seeing that twenty years ago Ormerod and Homén noted exactly the same pathological changes in their cases, I think it will be conceded that the term is amply justified. In any case, it may remain till subsequent investigation finds a better.

Progressive lenticular degeneration may be defined as *a disease which occurs in young people, which is often familial but not congenital or hereditary; it is essentially and chiefly a disease of the extrapyramidal motor system, and is characterized by involuntary movements, usually of the nature of tremor, dysarthria, dysphagia, muscular weakness, spasticity, and contractures with progressive emaciation; with these may be associated emotionalism and certain symptoms of a mental nature. It is progressive, and, after a longer or shorter period, fatal. Pathologically it is characterized predominantly by bilateral degeneration of the lenticular nucleus, and in addition cirrhosis of the liver is constantly found, the latter morbid condition rarely, if ever, giving rise to symptoms during the life of the patient.*

(2) Etiology.

(1) *Age.*—Of those patients whose cases have been recorded as instances of progressive lenticular degeneration, the age of the youngest at the onset of the disease was 10 years; of the oldest 26. The average age, calculated from the series of twelve cases, is 15. In the more acute cases the disease made its appearance at a relatively earlier age than in the more chronic cases, but that it is essentially a disease of adolescence may be definitely concluded from the material before us.

(2) *Sex.*—Of the twelve cases seven were males and five females. In no one of the seven male cases was there any sign of physical infantilism, as far as can be determined from the published records, and from observation in my own cases. Of the five female cases, one of the patients, in whom the illness began at the age of 17, had never menstruated; in the other four the catamenia were established before the onset of the illness; thereafter in each case menstruation became irregular or ceased—an interesting fact, the significance of which is at present obscure.

(3) *Heredity.*—In no one of the series was there any definite history

of family nervous disease such as could be considered to be of any significance. Such details as a neurotic temperament in a parent, or consanguinity of parents, or weak-mindedness in an uncle, or alcoholism in a grandparent's old age, are not sufficiently precise to be of value. Nor was there a history of any special diathesis in the families concerned. Both similar and dissimilar heredity may be excluded in the case of progressive lenticular degeneration.

It is a curious fact, however, that of the twelve cases of the disease here analysed for statistical purposes, no fewer than eight are familial cases, and it is also curious that the families concerned are large.

Thus in family K. (Homén) there were eleven children and one miscarriage; the first, third, and fourth were affected and died of the disease.

In family M. (Gowers, completed by Wilson) there were fourteen children and several miscarriages; the first, fifth, and eighth were affected.

In family P. (Wilson) there were six children and no miscarriages; the first and second were affected.

Passing next to the families in which only one member was affected:—

In family T. (Wilson) there were nine children and no miscarriages; the eighth child was the patient.

In family To. (Wilson) there were three children and one miscarriage; the patient was the youngest child.

In family S. (Ormerod) there were four children, but it is not stated in what order they came; one child was affected; there were one or two miscarriages.

In family J. (Ormerod, Wilson) the patient was the only child, and there were no miscarriages.

It is possibly of some importance that in all the familial cases the eldest members were affected, and that, on the whole, the elder members suffered while the younger escaped.

The exact significance of the familial element, however, is debatable and difficult. All that may be concluded from the fact that the familial element does enter largely into the disease, is that there may be some special predisposition which cannot as yet be expressed in more definite terms.

(4) *Distribution.*—It is premature to generalize where there are as yet so few recorded instances of the affection. For documentary purposes, however, it may be noted that the K. family belonged to Finland, and lived in the country; the M. family have always lived in

the East End of London; most of the P. family were born in Italy, of English parents; the T. family is English, and from the country, as is the To. family.

(5) *Predisposing causes.*—The generalities to which the observer in search of predisposing factors is too often driven need not delay us. It may once and for all be stated that in my own series of cases there is no record nor any evidence of syphilis as an etiological factor; and this is true also of the other reported cases. Homén made a most exhaustive examination of the members of his K. family, but was unable to obtain any definite or unequivocal data in favour of the syphilitic hypothesis. It is true that with the Wassermann reaction to aid us opportunity should be taken to apply it in any future instances of the disease; personally, I was not in a position to take advantage of it in the only two of my cases which I had the chance to examine after the test was demonstrated to be of value.

There is no evidence that alcohol may be considered to be a predisposing cause. One of the M. family suffered from typhoid fever seven years before the onset of the disease, and another had an attack of the same fever about a year before the appearance of lenticular symptoms. Yet these facts cannot be held to be of any importance.

Reference will be made in another section to the interesting circumstances that two of my patients (Cases 1 and 4) had an attack of jaundice some years before the lenticular symptoms were noticed.

(6) *Exciting causes.*—These are uniformly absent. It is recorded with almost complete unanimity that the disease came on apparently without any exciting cause, and in an insidious manner. Speculation, therefore, is useless.

One thing is certain, however, in the midst of much that remains obscure. In my own series of cases the patients were of normal mental and physical development before the onset of the disease, and the same remark is made by other observers. If the disease is the expression of a degenerative tendency, an abiotrophic defect—which I do not think at all probable—then it is curious that it should single out individuals who seem endowed with mental and physical gifts that are well up to the average, and who in earlier years have, without exception, given promise of full development.

(3) Symptomatology.

In progressive lenticular degeneration two clinical types may be distinguished, one acute or subacute, and the other chronic. Symptomato-

logically there is little difference between the two; the former is associated with some, it may be considerable, febrile disturbance, and the type of involuntary movements (which form a feature of every case of the disease) is not, perhaps, entirely identical with that of the more chronic cases.

Of the series of twelve cases, there are three which may be placed in the first category; in these the duration of the illness was four months, six months, and thirteen months respectively. In all, more particularly in the first, a high irregular temperature was present for a more or less lengthy period; emaciation was unusually rapid; the symptoms, speaking generally, were severe almost from the beginning, and the whole appearance of the patient suggested that he was seriously ill, as with a fever or any toxi-infective condition.

In the more chronic cases, of which there are nine, the patient's nutrition was well maintained, sometimes for a year or two; and he experienced a sense of well-being, for a long time at least, which was not belied by his looks.

In the main features of the disease, however, acute and chronic cases alike present a symptom-complex which is unmistakeable.

If we scrutinize the record to discover the earliest clinical symptom, there is none that is constant in this respect, and in several instances more than one symptom is recorded as having resulted in attention being drawn to the patient. In some, notably the K. family, the earliest symptoms were mental rather than nervous; in most, they were nervous rather than mental. Whatever be the first symptom to make its appearance, it is not long ere the disease establishes itself by a series of symptoms which have developed with astonishing similarity in all.

Progressive lenticular degeneration is a motor disease *par excellence;* its most striking and characteristic symptoms are disturbances of motor function.

(*a*) *Involuntary movements: Tremor.*—Involuntary movements, and in particular tremor, form one of the outstanding features of the affection. In all my own cases tremor was one of the earliest symptoms, as it was one of the most marked; in Homén's family tremor was equally pronounced, as in at least two of the M. family—i.e., in nine of the twelve cases. In the other three it does not appear to have been quite so prominent, although present.

In the recorded cases the tremor has been a true tremor—i.e., it has consisted of a regular, rhythmical, alternating contraction of a given muscular group and its antagonists. The rate is variable, usually within

the limits of four to eight times a second. It is increased, as a rule, by excitement, or if attention is drawn to it, or by voluntary effort. Thus it was always brought out well in the finger-nose test. At other times it appears to be to a certain extent under the control of the will, for by the exercise of volition it can be somewhat diminished for a moment or two, though this is by no means a constant phenomenon. Thus, when one of my patients grasped my hand tightly, the tremor with which the effort was at first accompanied became less as the patient's grasp increased in power; but, on the other hand, under these circumstances, the tremor was likely to appear as an "overflow" in some other place—e.g., the leg. Sometimes, when the patient was left entirely to himself, a perfect riot of tremulous movements could be observed. In most cases the tremor is more evident peripherally than proximally—i.e., it chiefly affects the fingers and hands, or the toes and feet, and it also usually affects these segments first. Thus bad handwriting was frequently remarked as one of the early signs of the disease.

The range of the tremor is usually fine, at least at the outset; with volitional movement the excursions become wider, and as the disease progresses the tremor, according to the experience of all the observers, becomes worse in every way. In one of Homén's cases, however, with increasing contracture the tremor rather diminished, but came in "attacks," in which the whole of the body was involved. In the later stages of the affection it is usually incessant, and involves head and trunk as well as the limbs. In one of my own cases I was able, by relaxing every joint and putting the limb into a position of complete muscular rest, to make the tremor disappear, but whenever the support was removed and the patient innervated his limb again the tremor reappeared and increased with great rapidity up to its maximum. As far as one can gather, it usually or always disappears during sleep.

In some of the cases the tremor has been less noticeable than in others, and in one or two it is reported to have affected the lower extremities more than the upper. The tongue is often tremulous, but this is not the tremulous fibrillation of such a condition as general paralysis; on the contrary, while the tongue is being protruded there is tremor, but when it is fully protruded the latter disappears.

In one or two of the old cases, what caught the eye of the observer was not so much tremor as "tonic" or "clonic spasms." Thus in the case of S. M. (Gowers)—one of the acute cases—both arms presented slowly changing tonic spasm, greater in the left. Sometimes

the movements were quicker, and they were always increased by an attempt at volitional movement. In the legs there were similar involuntary spasmodic movements, in the trunk, and indeed in the musculature generally. There were occasionally paroxysmal exacerbations of such spasms, of a few minutes' duration. In the case of W. S. (Ormerod)—another of the acute cases—the muscles were in a state of tonic spasm, and on the slightest forcible movement clonic spasms were produced. In the case of Alfred K. (Homén)—a chronic case—it is specially noted that, in addition to the tremors, "during the last few weeks of life tonic and clonic cramp attacks occurred, of short duration, at the longest a minute." On the other hand, in the case of C. M., the sister of S. M.—also an acute case—the involuntary movements were clearly of the nature of tremor, properly so-called.

It may be said, then, that in the chronic cases tremor was constantly present, and was pronounced and continuous; in two of the acute cases "tonic and clonic spasms" were met with; in the other acute case the movements were those of tremor.

(*b*) *Spasticity*.—Every one of the series of cases has been characterized by the presence of rigidity or spasticity, which has often reached an extreme degree. It has always been steadily progressive, and has resulted in the patient being reduced to a state of utter helplessness, unable to use his hands, unable to turn in bed, unable to recover his balance if that were disturbed. As a rule it has begun in the limbs, and in the cases which I have had opportunities of observing it has been more pronounced at the larger joints, possibly because here the muscles are naturally stronger and larger. The simplest way to convince oneself of the existence of this hypertonicity is to take one of the limbs, say the arm, and to impress on it passive movements of alternating flexion and extension at the elbow. Whichever be the movement made by the observer, he is always conscious of a considerable degree of resistance in the opposing muscles, so that quick passive to-and-fro movement of the forearm is an impossibility. The muscles always feel firm on palpation, and even when the limb is put into such a position as to relax any given muscle as far as possible, it can always be felt to be in a state of hypertonicity. Hence ensues an extraordinary degree of immobility in the advanced cases; the face is fixed, expressionless or smiling stiffly, and has consequently been noted as being "silly" or "fatuous." The head and neck are equally fixed; even in the recumbent position the sternomastoids are not relaxed. The rigidity of the trunk

is such that maintenance of equilibrium becomes a matter of the greatest difficulty. As one of my patients was sitting on the edge of his bed he slowly fell backwards in a helpless fashion, with his legs in the air, quite unable to relax his hypertonic muscles or to use them to recover his balance.

As a rule the predominant hypertonic muscles are the flexors, though to this there are certain exceptions. In most instances the fingers and wrists are flexed, the elbows flexed, the arms adducted at the shoulders; the toes are curled under the feet, the feet turned in, the heels drawn up, the legs flexed at the knee and hip. In one of Gowers's cases, however, the limbs were extended at the knees, and at the elbows, and the arms were rotated inwards so that the palms looked back and outwards. It would appear that even in sleep the rigid condition of the musculature does not alter.

It is important to note, as will already have appeared, that in these cases we are dealing with a true hypertonicity of the muscles, involving both synergic and antergic muscles simultaneously. The rigidity is not due merely to inability to relax an antagonist, or to predominant flexor tonicity. As far as can be seen there is a generalized condition of increased tone in all the muscles indiscriminately, and the fact that this tonicity leads as a rule to the adoption of a flexor attitude is for the present immaterial. (*See* also Chapter VI.)

The solitary muscles of the body that do not appear to be implicated in this condition are the extrinsic ocular muscles. In my own cases their volitional movements were quick and free. Gowers, however, records that in the case of S. M. the movements of the eyes were normal, but at times the eyeballs rolled upwards. Ormerod remarks that in his patient the right eye " worked," but possibly this means that the muscles round the right eye were involved in the spasm which implicated the right side of the face. In the case of D. P. there were involuntary rolling movements of the eyes a few days before death—not a point of any special significance. Otherwise no voluntary muscle or group of muscles seems to be exempt. In my opinion the dysarthria and dysphagia, if not wholly, at least in great part, must be attributed to this rigidity. The open mouth of the patient provides a striking exemplification of his mental attitude in regard to this rigidity. If fig. 2, taken in 1886, is compared with fig. 21, taken in 1910, one cannot fail to note the indifference to the fact as expressed in the patient's face. He seems to be as unaware of the spasmodic depression of his inferior maxilla as he is indifferent to his tremor or oblivious of his sialorrhœa.

(*c*) *Contractures.*—It is but a step from rigidity to contracture. Contractures are as constant a feature of progressive lenticular degeneration as the involuntary movements. It is remarked of every patient that his or her limbs were grossly contracted towards the end. The contractures generally begin in the distal segments of the limbs, as exemplified in various figures which have been given in the clinical section. As the disease progresses so do the contractures, until they become extreme. It may be impossible to straighten the limbs out; two stages in the process may be noted, and two causes in its production. The first is the fixation of a limb in a particular position from hypertonicity of the musculature. This first stage is well illustrated by my Case 3. The patient looked as though his limbs were contracted up in the attitude of double hemiplegia or of paralysis agitans, but by dint of passive movement it was possible to extend them almost completely. This first stage is one of contracture-attitudes from hypertonicity, a purely nervous phenomenon. But secondly, as the result of the prolonged maintenance of fixed attitudes, myogenic contracture sets in, owing to permanent approximation of the origin and insertion of the muscles. This naturally shows itself most in those muscles which have caused the adoption of a given contracture-attitude: hence if this be one of flexion, the flexion contracture is accentuated, and the limb gets into a distorted condition from which no amount of passive movement can correct it. Thus we read that in one case the knees were right up on the patient's abdomen; in another the lower extremities were flexed at all joints; in a third the arms were permanently contracted at the finger-joints, wrists, and elbows; and so on.

It is apparent, of course, that "tonic and clonic spasms," spasticity or hypertonicity and contractures, are pathological conditions intimately allied to each other. Their pathogenesis will be discussed later, but at this point it is well to mass them together, as they may be present in varying degree in any given case of the disease, and it is desirable to realize that this possible variability, so far from confusing the diagnosis, is really to be expected from the nature of the affection.

(*d*) *Dysarthria; dysphagia.*—Dysarthria has been present in every one of the series of twelve cases, and in all it has advanced until it has resulted in more or less complete anarthria, the patients being unable to articulate intelligibly a single word or syllable. The dysarthria is characterized by the slurring element, without the staccato element, of the speech of disseminated sclerosis; the greatest difficulty is with certain consonants, and there is a frequent tendency to

abbreviate the ends of words. When at its worst the patient may still be able to phonate though articulation is impossible, hence unintelligible sounds may issue from the throat. Homén, Gowers and Ormerod have remarked on involuntary noises, or sounds, or moans, escaping from the patient. In my own cases this was not perhaps quite so marked.

The defect is in no wise comparable to that of general paralysis, and so far from there being facial overaction, as in the latter condition, the sounds escape from a mask-like, immobile face and mouth. Reference is made in a subsequent section to the variability in the dysarthria from time to time.

Dysphagia is as constant as dysarthria, and in a majority of the cases the two conditions have come on simultaneously.

(*e*) *Muscular weakness and emaciation.*—While progressive emaciation has marked the course of the disease both in the acute and the chronic cases, there is no record of local muscular atrophy. The wasting affects the musculature generally, and is associated, partly at least, with the contractures and the immobility of the limbs. Atrophy from disuse is a well-recognized condition. At the same time, some of the emaciation may very well be attributed to profound disturbance of metabolism, especially in the acuter cases, where, although the duration was shorter, the degree of wasting was, if anything, more severe.

In spite of the tremors, rigidity, and contractures, in the majority of the recorded cases a degree, and sometimes a considerable degree, of voluntary power has remained. Several of the previous writers have been struck by the apparent incongruity between the two facts, and the significance of the contrast will be discussed in the section on the pathological physiology of the disease. It is sufficient to note at present that in the early stages, at least, considerable muscular power may be retained, and voluntary movements may be of normal range, even though the patient gives the appearance of helplessness. In each of my own four cases the patients were still able to walk at a time when their appearance suggested complete spastic paralysis.

Muscular weakness, however, is undoubtedly one of the symptoms of progressive lenticular degeneration. Volitional movements may be good in range but they are usually resisted with comparative ease. This muscular weakness, also noted by previous observers, is not to be confused with clumsiness or awkwardness from hypertonicity or tremor. There is intrinsic muscular asthenia; the patient is incapable of any sustained effort; he cannot close his eyes tightly for any length of time, cannot keep his tongue protruded, cannot maintain his grasp. It may

be said, without risk of being misunderstood, that volitional innervation is defective, while involuntary innervation is exaggerated.

Admitting, however, the muscular weakness, one ought not to use the term "paralysis" to express it. The condition is one of muscular weakness without paralysis. "Paralysis," where motion is concerned, ought to be confined to diseases of the pyramidal system. In the case of progressive lenticular degeneration the motor symptoms are foremost, but except where contractures or rigidity forbid it the patient is able to move his limbs. Although the lower facial musculature looks immobile, the hypertonicity can sometimes be overcome sufficiently, and the patient will move his lips. He is not, therefore, "paralysed." There is no special term to indicate this specific motor helplessness resultant on disease of the extrapyramidal motor system.

(*f*) *Sensory.*—Compared with the motor, the sensory symptoms are minimal. On the subjective side, Homén observes that his patients suffered from occasional pains in the body and limbs, more especially the legs, and mainly at the beginning of the disease. Ormerod states that his patient had at one time paroxysms of pain, evidently associated with spasmodic contractions of the muscles, akin no doubt to painful cramps. The importance of these it is difficult to gauge; in any case the symptom is far from common and may be relegated to a secondary place. On examination no change in sensibility is discoverable. All of my four cases were carefully examined from the sensory standpoint, with a negative result. There are no sensory symptoms in pure lenticular disease.

(*g*) *Reflexes.*—In a pure case of the disease, such as my Case 3, there is no definite alteration in the tendon reflexes; they are active, but not exaggerated. Exaggeration of the reflexes is not a sign of lenticular degeneration in its uncomplicated form. It not infrequently happens that owing to the contractures they are elicited with difficulty. There is no ankle or other clonus. From the point of view of the cutaneous reflexes the only cases which have been examined with the help which knowledge of the significance of the plantar reflexes gives are my four personal cases. Of these, Case 1 had an extensor response on one side, but in view of the undermining of the internal capsule this is easily accounted for. Nevertheless, it must be remarked that in that case there is no descending degeneration in the pons, medulla, or cord. In Case 1, moreover, the abdominal reflexes were diminished on both sides. In Cases 2 and 3, which, clinically, be it observed, were just as severely affected as Case 1, the abdominal reflexes were normal—in

Case 2 they were readily obtained a few days before death—and there was a double flexor response. At the time when I last examined the patient whose case is No. 3, his condition was every whit as advanced as was that of Case 1, yet the state of the cutaneous and deep reflexes precluded the possibility of organic disease of the pyramidal tracts. In Case 4 the "boarding" of the abdominal muscles was no doubt the cause of the diminution or absence of the abdominal reflexes. A double flexor response was obtained. These facts are of primary importance from the standpoint of pathological physiology.

In every case of the series the organic reflexes are recorded as having being impaired towards the end; in fact, most of the patients have in the latest stages become "wet and dirty." This is not to be taken as indicating local sphincter-defect such as one meets with in disease of the lower part of the cord (the spinal cords were throughout normal); on the other hand, I am not sure that it ought without further consideration to be attributed, as some would have it, to the mental deterioration of the patient, and to be interpreted as a sign of dementia. It seems to me that it may very well be due, in part at least, to increasing imperfection (of central origin) of voluntary control over the muscles concerned.

(*h*) *Mental symptoms.*—Of considerable interest are the psychical symptoms of progressive lenticular degeneration. It is a noteworthy fact that some form of mental change or impairment is specifically referred to in at least eight of the twelve cases; its importance, therefore, must not be underestimated. On the other hand, this mental impairment is highly variable both in degree and in kind, and therefore calls for some analysis.

Of Gowers's two patients one did not represent any definite mental symptoms; at least they are not referred to as such. The other is said to have been listless, lethargic, emotional, and easily excited to laughter. Ormerod's patient seemed "silly"; he became noisy and apparently idiotic; "his mental condition seemed to get worse, and he lay howling all day long." Homén's three cases were all characterized by what he calls "dementia." The symptoms he mentions may be thus generalized: listlessness, slowness of mental processes, "simple-mindedness," failure of memory and of mental powers, emotionalism, stupid and idiotic facial expression, &c. My own first patient evinced a change in her disposition; at first she was restless and unable to settle to anything; she was easily provoked to laughter, her manners were childish, her mental powers to a certain extent diminished; but, on the other hand, her

memory remained good, at least for a long time after the disease was established, and on the receptive side little defect was observable. In Case 2 the earliest symptoms were that the patient became rather untidy in her dress, failed to obtain the same number of marks at school as formerly, later developed transient delusions, became emotional, and was easily provoked to laughter; "her younger sister had to be a mother to her," such was her childishness. In Case 3 the first symptoms were those of a moderately severe toxic or exhaustion psychosis, consisting in delusions, hallucinations of hearing, excitement, &c. They passed off entirely, never to return, but within a year the characteristic symptoms of progressive lenticular degeneration made their appearance, and in the case of this patient similar mental changes (though less in degree) to those already described in the case of his sister subsequently occurred. He was emotional, childish, facile; yet here also, while undoubtedly there was impairment of mental power, to some extent, on the afferent side no defect was to be seen. His memory and powers of recognition were for a long time unimpaired; his observation and perception were astonishingly quick. In the case of C. J., my Case 5, instead of remaining bright and intelligent, he became dull and stupid; he was very emotional, at one time laughing, at another crying; he was slow in answering questions, and in understanding everything that was said to him; but, on the other hand, he did everything correctly that he was asked to do. At the same time, it must be remembered that in my Case 4 no mental change is at present noticeable, and this has been the case in some of the earlier recorded instances of the disease.

In view of the frequency, then, with which some one or other psychical symptom is encountered in the disease, I am inclined to admit they form an important, though perhaps not an integral part of the clinical picture. An endeavour to specify the cardinal element or elements in them, or to classify them, is a matter of some difficulty. If the term "dementia" is to be employed to characterize them, it must not be forgotten that this dementia is decidedly limited. I carefully examined all of my patients from the point of view both of agnosia and of apraxia, but in no one of them were these symptoms present. Now it is just in the ordinary dementia of senility, of general paralysis, and to a less extent in dementia præcox, that these symptoms are most common, especially in the first of these. Hence the term "dementia" is not really appropriate. Disorientation in time and space is another of the common features of dementia, but in more than one

of my cases, if present at all, it was slight. The "dementia" of progressive lenticular degeneration cannot be likened to the steady mental involution of senile dementia, or of dementia paralytica, and it can be readily distinguished from dementia præcox.

The mental defects in the disease, when present, may occur in one or more than one of the following forms:—

(1) *Narrowing of the mental horizon.*—The patient does not seem to be able to add much to his store of mental images, and his capacity for retaining impressions is impaired; but within the limits of this constricted mental field his powers of perception and recognition are good. There are no delusions or hallucinations, as far as can be determined; and the mental condition does not deteriorate or degenerate *pari passu* with the physical condition of the patient. In Case 3 the patient, even *sub finem*, was perfectly cognizant of what was going on round him and was able to reply to questions by rational gestures. In one or two respects the mental condition is not unlike what may be seen in the early stages of Huntington's chorea.

(2) *Facility, docility, and childishness.*—The patient, especially as the disease is advancing, often becomes easily tickled, pleased, amused. Apparently he has no insight into his condition, for his cheerfulness is incompatible with knowledge of the seriousness of his illness. Some patients have not shown this euphoria, which, for that matter, is found probably only in chronic cases. The patient seems to be unable to deliberate or pass judgment on what is presented to him. Increase of emotionalism and of emotional reaction is not infrequently observed. Sometimes a condition resembling "rire spasmodique" is met with, never "pleurer spasmodique." This involuntary laughter is no doubt associated with the disease of the basal ganglia. (*See* below, p. 477.)

It may, however, be again remarked that some cases do not show much or any obvious mental change, while others present mental symptoms that are unique as far as each individual case is concerned.

(*i*) *Symptoms referable to other systems.*—The only system to which reference need be made is the alimentary. Homén's patients suffered from occasional sickness, one of them from frequent vomiting. All had loss of appetite as one of the initial symptoms. Neither Gowers's nor Ormerod's patients showed any gastro-intestinal symptoms, if we except what seems to have amounted to bulimia in the latter case, at one stage of the illness. No one of my patients presented any symptoms referable to the alimentary system, except Case 1 *sub finem*. With the exception of the case of C. J., No. 5 in my series, not one of the

patients was found during life to have definite symptoms or signs of disease of the liver—i.e., while lenticular symptoms were present. In Case 1 of my series it may be remembered that an attack of jaundice occurred some years before the onset of the lenticular disease, and this patient suffered from severe hæmatemesis just before death; similarly, in Case 4 there was a history of an attack of jaundice some years before the onset of the lenticular symptoms.

It is a remarkable fact that in ten cases advanced hepatic cirrhosis has been found on *post-mortem* examination when symptoms of it during life have been conspicuously absent.

(*j*) *Negative signs.*—If negative signs are ever of any value certain of them may be tabulated here.

In progressive lenticular degeneration: The optic discs are normal; the pupillary reactions are normal (in only one case were the pupils said to be sluggish to light); there is no nystagmus; the palate moves on phonation and reflexly; there is no fibrillation or localized amyotrophy; there are no cerebellar symptoms; there is no impairment of sensibility; the reflexes are not those of pyramidal disease.

There are certain general features in the symptomatology of the disease to which attention must be directed, as they help to an understanding of the condition. These are, briefly, the pronounced variability in the symptoms from time to time, and the resemblance which some of them may present at a certain stage to what is called "functional" disease. A discussion on these points will be raised in a subsequent section (p. 459).

(4) Pathology.

In analysing and synthetizing the pathology of ten cases of progressive lenticular degeneration, the first point to draw attention to is that in three cases the examination of the central nervous system proved negative—viz., S. M. and C. M. (Gowers) and C. J. (Ormerod, Wilson). On the other hand, in the case of W. S. (Ormerod), Homén's three cases, and three of my own cases, symmetrical bilateral lenticular degeneration was found—i.e., in seven out of ten cases, a sufficiently large proportion to justify one in expressing the opinion that a minute microscopical examination of the corpus striatum in the other three, the negative, cases, might have revealed some pathological changes. In the case of S. J., only a macroscopical examination of the brain was made, apparently, and it was negative. In the cases of

S. M. and C. M. " pieces of the cortex, cord, nerves and muscles," were examined microscopically, with a negative result. There is no reference to a microscopical investigation of the basal ganglia. Now in view of the fact that in these very structures—viz., cortex, cord, nerves and muscles—examined in each of my three personal cases with modern histological methods, no definite changes of any significance could be detected, it is little wonder that the examination of twenty-two years ago was negative. The point is that in the acute cases it is quite possible the only lenticular change may be a microscopical one, if indeed it is to be seen at all. We have the evidence of Ormerod's case (one of the acute cases) to show that pathological changes in the lenticular nucleus may be recognized after a few months; on the other hand, in the case of C. M. the duration was thirteen months, and a priori, had any naked-eye lenticular change been present it was sure to have been detected. An argument by analogy from two of my series—viz., Case 1 and Case 3—may be stated in this connexion. In the former the pathological changes were much more advanced than in the latter, yet clinically no such difference in degree obtained. Hence, we must not judge of the severity of the clinical symptoms by the degree of pathological and structural change found at the autopsy. Accordingly, it may fairly be held in the case of C. M. that the function of the corpus striatum may have been dynamically disturbed without much structural change being recognizable.

In the seven cases with positive findings in the central nervous system the appearances are so similar that they afford striking proof of the selective action of some morbid agent. In all, with the exception of my Case 2, where the examination was incomplete, but where the assumption that the case was identical with the others is abundantly justifiable, there is bilateral symmetrical degeneration of the putamen, and of the globus pallidus to a less extent. Various degrees of this degeneration are found, from discoloration and sponginess of the nucleus, through shrinkage and atrophy to complete disintegration and excavation of the ganglion. Neighbouring structures are involved to a much less extent; the caudate is often rather shrunken, but never disintegrated as is the lenticular nucleus. The optic thalamus is practically always normal, except in so far as loss of striothalamic fibres may affect its lateral part (" zone grillagée " and lamina medullaris externa); and in pure cases the internal capsule is intact from end to end. Sometimes the external capsule is degenerated, mainly in its middle or posterior third; the claustrum is usually normal, and the convolutions of the island of

Reil normal, though sometimes the latter show diminution of cortical fibres, and a certain slight loss of substance. Apart from the degeneration in the lenticular nucleus, the changes in the brain are insignificant. There is no evidence of established meningitis; sometimes slight leptomeningeal thickening is found, patchily distributed. The cerebral cortex offers little definite alteration; Homén found the frontal cortex possibly somewhat thinned, with slight diminution of myelinated fibres, but there is no wholesale chromatolysis (by Nissl's method) in any of the modern cases; on the contrary, and more particularly in the motor area of the precentral convolution, the cortex is practically normal. The Betz-cells are well up to normal numbers and stain well. There is no sign in the modern cases of any small-cell infiltration anywhere; Homén found slight traces of this in his cases, but remarks that it is nothing like so pronounced as is met with in dementia paralytica; Ormerod found small-cell infiltrations in the lenticular nucleus in his acute case.

The microscopic changes in the lenticular nucleus in the chronic cases are not, however, accompanied by small-cell infiltration. They consist of glial overgrowth, which afterwards disintegrates and breaks down; there is often an immense increase in glial nuclei; the nerve-fibres and nerve-cells of the normal nucleus disappear; "Körnchenzellen" and macrophages are frequently present in numbers. Even when the cavity formation is extreme there are no signs of obliterative endarteritis in the blood-vessels, the perforating lenticulo-striate vessels and their branches; on the contrary they are, if anything, thinned, and are sometimes hyaline. Very occasionally their adventitia seems thickened; the intima never. Round the vessels gaping spaces make their appearance, possibly from shrinkage of the nervous tissues, hence the nucleus presents a finely worm-eaten appearance; this is a stage previous to cavitation. In Homén's cases more definite disease of the blood-vessels was found than in my cases. He notes that they were irregularly sclerotic—i.e., had patches of degeneration in their walls, with small collections of granular material between the coats of the vessels; sometimes the granular material bulged into the lumen of the vessel. Sometimes they were the seat of hyaline degeneration. The intima, nevertheless, is not stated to have been pathologically altered. Changes of this kind he found in all his cases, nor were they confined to the arteries of the basal ganglia.

The pons, medulla, and cord are uniformly negative from the pathological point of view, any changes which they may present being of secondary importance. This is true also of the nerves and muscles.

In the modern cases certain degenerations consecutive to the main lenticular disease can be traced. These are, in advanced cases,

degeneration of the ansa lenticularis, relative atrophy of the corpus Luysii, partial degeneration of the lenticular bundle of Forel and of the strio-Luysian fibres, and degeneration of striothalamic fibres.

Two other organs are commonly affected in this disease—viz., the liver and the spleen. The liver is always cirrhosed, from hepatitis, and I do not think a diagnosis of progressive lenticular degeneration can be made in any case in which the liver is not thus affected; in other words, I consider it is essential. In several of the cases the spleen is reported as having been enlarged, but without any other change. The exact significance of this is at present obscure.

The cirrhosis of the liver is always advanced, and strikingly apparent. The organ is usually rather smaller than normal, but not constantly so. It is firm, hard, tends to preserve its shape, and presents the appearance of rounded nodules of liver-tissue clustered together, of the size of hazel-nuts or larger, separated by depressed cirrhotic bands. The organ is never bile-stained, but is often rather lighter in colour than usual. Microscopically are found normal areas, necrosed areas, fattily degenerated areas, and actively regenerating areas, scattered irregularly through the organ. The type of cirrhosis is mixed—i.e., it is mostly multilobular, in some places monolobular, and occasionally there are indications of intralobular cirrhosis. So-called hypertrophying bile-ducts are often seen in the new connective tissue formation. Finally, this cirrhotic new formation is often very narrow, and in some places is very cellular, in others more fibrous.[1] In certain of my own cases the pituitary and suprarenal were apparently normal, as was the kidney; the thyroid showed regressive and proliferative changes.

(5) Diagnosis.

To anyone familiar with the disease its symptomatology and course must appear so characteristic that he may well think it a *morbus sui generis*. It offers so many features that are almost unique, that it is difficult to see how confusion might arise. The acute cases, for instance, which run a course of a few months, are in my opinion really unique. They do not offer analogies with any other nervous condition with which I am acquainted.

Of the affections with which progressive lenticular degeneration

[1] Several questions in reference to the occurrence of hepatitis in young people, and in families, and in reference to the exact nature of the cirrhosis in progressive lenticular degeneration, will be discussed in a separate communication.

might conceivably be confused, disseminated sclerosis may first of all be mentioned. Yet the resemblance is but superficial. In the former there are no nystagmus, optic atrophy, amblyopia, paræsthesiæ, objective changes in sensibility, absence of the abdominal reflexes, extensor responses and ankle-clonus. The dysarthria in the two affections is not identical; the rigidity of disseminated sclerosis is rarely, if ever, so universal or complete as in the other; contractures do not form so essential a feature of the symptomatology. The course of disseminated sclerosis is much more variable and very often longer in duration. It is only in the early stages that confusion is possible, when there is as yet absence of organic signs, so called; a patient who suffers from intention-tremor and slight dysarthria is certainly difficult to place when other signs fail.

The differential diagnosis from bulbar palsy should present no difficulty, and need not be enlarged upon. Pseudobulbar paralysis, however, may be more difficult to distinguish. Pseudobulbar paralysis is a disease of the pyramidal tracts, of that section of them which goes from the lower part of the motor area via the genu of the internal capsule ("faisceau geniculé") to pontine and bulbar motor nuclei. The result of bilateral (much more rarely unilateral) involvement of these fibres is the production of dysarthria, dysphagia, inability to protrude the tongue, paralysis of the palate, paralysis of the lower part of the face, sialorrhœa, often involuntary laughter, &c. Such a clinical picture of course in some ways resembles, so far as it goes, that of progressive lenticular degeneration. There is a further complication. The fibres from the operculum, forming the "faisceau geniculé," run partly in the external capsule, and skirt the lenticular nucleus (without, however, actually passing through it except to a very slight extent at its upper and anterior extremity) on their way to the genu of the internal capsule. It may therefore be questioned to what extent a large lesion of the lenticular nucleus, especially if the external capsule be to any extent implicated, must not of necessity involve some of the geniculate fibres, and, if it is bilateral, thus occasion a degree of pseudobulbar palsy, apart altogether from the true lenticular symptoms; the latter, coming on top of the former, may not easily be distinguished, if at all. I believe that in one or two of my cases (especially of course Case 1), the geniculate fibres were involved to some extent, apart from the lenticular disease. In Case 3, however, the genu is apparently intact on both sides, and if the geniculate fibres are at all affected directly, this can only be through some involvement of the external capsule.

In typical pseudobulbar cases the palate and tongue are paralysed. In progressive lenticular degeneration they are only apparently paralysed; the palate moves on phonation, and the tongue can be protruded, if slowly. In other words, in pure cases of the disease the dysarthria, dysphagia, &c., are the result of the rigidity of the motor mechanisms concerned, comparable to the rigidity of the general skeletal musculature. As the disease progresses, should the geniculate fibres become involved, the clinical picture will change, though the process will not be easy to detect, to that of true pseudobulbar palsy. As a rule, cases of the latter condition present symptoms of double hemiplegia, and the condition of the reflexes will serve to distinguish the hemiplegia from the "paralysis" of progressive lenticular degeneration.

Paralysis agitans is a disease in several ways closely resembling progressive lenticular degeneration. The age of onset in the former, however, is by itself almost sufficient for differential diagnosis. The latter is a disease of youth. Paralysis agitans is very much more chronic, and speaking generally the attitudes of that disease are just as specific, in their own way, as those of the other, from which they differ considerably. The question of the analogies between the two will be discussed in a subsequent paragraph (p. 479).

Juvenile general paralysis may be mentioned, only to be dismissed.

(6) Duration and Prognosis.

The experience of all who have had opportunities of following the course of the disease is that it is invariably fatal. It may be remarked, however, that in most of the cases the diagnosis was not made till the patient reached the *post-mortem* table, and it is conceivable that cases of the disease, which have not, however, been recognized, may have recovered; nevertheless, I do not think this probable. The trend of the affection is always steadily downwards; remissions are so insignificant as scarcely to be worth the name. The outlook, once a diagnosis is made, is always serious and may at any time become grave. The duration of the three acute cases was four, six and thirteen months respectively. The shortest of the more chronic cases lasted two and a half years; the longest case on record is one of Homén's, which went on for seven years. The average duration of the first three of my cases is three and a half years. The average of eight chronic cases is almost exactly four years.

TABLE SUMMARIZING ALL THE KNOWN CASES OF PROGRESSIVE LENTICULAR DEGENERATION.

Number	Initials	Author	Year when case came under observation	Sex	Familial or otherwise	Age at onset	Duration of illness	Result and age	Symptomatology				Pathology					Number
									Motor system	Sensory	Reflexes	Mental	Brain	Cord	Liver	Spleen	Other findings	
1	Sl. M.	Gowers, Wilson	1879	M.	Familial	10 yrs.	4 years	Death at 14	Anarthria, dysphagia, contractures, emaciation, "limbs constantly on the work"	*Nil*	Not known	*Nil*		No *post-mortem*				1
2	Sy. M.	Gowers	1886	M.	,,	10 ,,	4 months	,, 10	Anarthria, dysphagia, contractures, emaciation, "tonic and clonic spasms"	,,	Plantars "slight," abdominals absent, knee-jerks present	,,	Nothing definite found	Normal	Cirrhosis	Not mentioned	..	2
3	C. M.	Gowers	1888	F.	,,	15 ,,	15 ,,	,, 16	Dysarthria, tremors, spasmodic contractures, emaciation	,,	Knee-jerks present, later absent (? from spasm)	Emotional	,, ,, ,,	,,	,,	,,	..	3
4	W. S.	Ormerod	1889	M.	—	10 ,,	6 ,,	,, 10	Anarthria, dysphagia, contractures, emaciation, rigidity, "clonic spasms"	Pains in limbs	Knee-jerks active	Emotional, "idiotic," "howls vehemently"	Bilateral softening of putamen	,,	,,	,,	..	4
5	C. J.	Ormerod, Wilson	1889	M.	—	11 ,,	2 years	,, 13	Dysarthria, muscular weakness, contractures, rhythmical tremors and spasmodic contractions, emaciation	*Nil*	Knee-jerks active, abdominals present, plantars "brisk"	Emotional, dull, stupid	Nothing definite found	,,	,,	Large, firm, congested	..	5
6	Ad. K.	Homén	1889	M.	Familial	20 ,,	3 ,,	,, 23	Stiffness, weakness, anarthria, dysphagia, contractures, rhythmical tremors, "tonic and clonic cramps"	Pains in limbs	Cutaneous reflexes "weak," tendon reflexes difficult to test	Dull, listless, "simple"	Bilateral lenticular softening, irregular thickening of membranes in some places, slight frontal convolutional atrophy	,,	,,	Normal	Slight sclerotic or hyaline changes in smaller cerebral blood-vessels	6
7	W. K.	Homén	1888	M.	,,	12 ,,	7 ,,	,, 19	Rigidity, weakness, contractures, tremors, anarthria, dysphagia, emaciation	Pains in limbs	Tendon could not be tested, cutaneous "weak"	"General appearance suggested dementia"	Bilateral lenticular cavitation, very slight frontal and central convolutional atrophy	,,	,,	Enlarged, firm	Small localized granular and hyaline changes in cerebral blood-vessels	7
8	Aa. K.	Homén	1888	F.	,,	20 ,,	6 ,,	,, 26	Stiffness, weakness, tremors, anarthria, dysphagia, emaciation	Pains in limbs	Not mentioned	Apathetic	Bilateral lenticular softening, slight irregular thickening of membranes	Not mentioned	,,	Normal	A few circumscribed endarteritic changes in certain cerebral blood-vessels	8
9	S. T.	Wilson	1905	F.	—	26 ,,	4½ ,,	,, 30	Anarthria, dysphagia, rigidity, contractures, weakness, emaciation, rhythmical tremors	*Nil*	Abdominals dim., knee-jerks present, plantars at first flexor, later extensor L.	Emotional	Bilateral lenticular cavitation, internal capsule slightly implicated L. genu	Normal	,,	Firm, congested	Slight changes in thyroid	9
10	D. P.	Wilson	1906	F.	Familial	17 ,,	2½ ,,	,, 19	Anarthria, dysphagia, rigidity, contractures, weakness, emaciation, rhythmical tremors	,,	Abdominals present, plantars flexor	Emotional, facile, transient toxic psychosis symptoms	Right lenticular degeneration (and probably also left), internal capsules normal	,,	,,	Enlarged	..	10
11	E. P.	Wilson	1907	M.	,,	19 ,,	3 ,,	,, 22	Anarthria, dysphagia, rigidity, contractures, weakness, emaciation, rhythmical tremors	,,	Abdominals present, plantars flexor	Emotional, facile	Bilateral lenticular degeneration, internal capsules normal, slight patchy thickening of membranes	,,	,,	Enlarged, firm	Changes in thyroid: pituitary and suprarenal normal	11
12	M. To.	Wilson	1911	F.	—	18 ,,	Still living, aged 20 years		Anarthria, dysphagia, rigidity, contractures, weakness, emaciation, rhythmical tremors	,,	Abdominals not obtained (? from rigidity), plantars flexor	*Nil*	Still living					12
13*	C. Z.	Frerichs	1854	M.	—	9 yrs.	About 1½ years (?)	Death at 10	Dysarthria, dysphagia, weakness, tremors, slowness of muscular movement	*Nil*	Not mentioned	Apathetic	"Membranes injected and substance of brain soft" (P. died from acute dysentery)	Not mentioned	Cirrhosis	Enlarged	..	13

* Not included in the cases here analysed. For description of case, see footnote p. 319.

(7) Treatment.

What can be said of the treatment of the disease? Its nature must be discovered before treatment can be lifted from the empirical to the rational level. All that can be done by those who have had charge of cases is treatment of an essentially symptomatic and palliative kind. In my Case 4, at present under observation, I am trying the effect of urotropine, administered over a long period of time.

Chapter V.—Nature and Pathogenesis of the Disease.

When we leave the realm of facts to face the problem of the nature and pathogenesis of progressive lenticular degeneration, difficulties begin. The first impression of the disease is that it is so different, apparently, from most familiar morbid types, as to constitute a class by itself, and that there is no other affection with which to compare it. It is true that this disease is, I believe, the first definitely established morbid entity whose most striking characteristic is a specific association between disease of one of the viscera and disease of a particular part of the grey matter of the central nervous system—viz., the lenticular nucleus. The mystery, however, is perhaps not so impenetrable as may at first appear. There are certain symptoms of the disease which furnish a clue to its nature, and further, there are certain analogies to be drawn from other diseases, as will shortly be seen, which will aid materally in the attempt to explain its pathogenesis.

First of all, the opinions of the older writers may be quoted. To the clinical acumen of Gowers, Ormerod, and Homén, the student of the disease is greatly indebted, for each, recognizing he was dealing with a disease *sui generis*, examined his cases and published the record with a fulness of detail which leaves nothing to be desired. I count myself fortunate to have had access to the original notes of some of these cases, for a link is thus formed between the old and the new which enhances the scientific value of each.

Gowers, the observer of the earliest cases, writes as follows [4] :—

"In the two cases I have recorded no symptom of inherited syphilis was present. The probability of inherited syphilis as the cause of the malady of the nervous system rests entirely on the significance of the hepatic cirrhosis, whether or not syphilis is the only cause of the juvenile non-alcoholic form. Even the assumption of this causation leaves the direct pathology as mysterious as before. It is inconceivable, in the first case, and most improbable in the second, that any coarse

morbid process could have existed and have escaped the careful examination to which the nerve-centres were subjected. The facts seem compatible only with a blood state as the cause of the symptoms.

"But if a blood state caused the symptoms, the question arises: Were this and the cirrhosis of the liver the common effects of one cause, or can the blood state have been the effect of the hepatic disease? Anomalous as the last assumption may seem, it cannot be hastily dismissed. In connexion with the difference in the character of the symptoms, there is also the association of the higher fever in the second case with a greater degree of disease of the liver. Toxic blood states may be complex in causation; one derangement of the chemical processes of the system may induce others, the effects of which co-operate with the first."

Ormerod [7] makes the following remarks, in addition to what has been already quoted from his paper:—

"The German cases which we shall quote presently make it probable that the softening in the neighbourhood of the lenticular nuclei had some essential connexion with the disease; but it will hardly explain the whole course of symptoms. . . . Professor Homén apparently would explain the whole of these morbid appearances as being due to inherited syphilis, though there was no clinical evidence of this. Upon the intimate nature of the disease, however, an opinion can hardly be given till more observations have been made. . . . Whether it is right to put the cirrhosis of the liver in as prominent a place as I have done in the heading of this paper, must be judged by the comparison of other similar cases, but I think it can hardly be counted as a coincidence."

Homén [6], in the course of his remarks on the pathogenesis of the disease, says that everything points to the vessel-degeneration as the primary lesion. As there was no sign of acquired syphilis in his patients, and indeed, apparently, no possibility of its having been acquired, Homén is driven to the conclusion that the syphilis, which he postulates for the vessel-degeneration, must be congenital or hereditary. Yet he is doubtful himself about his own contention. In cirrhosis of the hereditary syphilitic type the pathological picture is different from that of his cases, and clinically the presence of ascites is practically constant, whereas it was absent in all of them. He concludes in the following guarded terms:—

"If we consider, finally, all the pros and cons, we must conclude, taking all the circumstances into account, that even though positive evidence is wanting, yet in all probability we are dealing with an unusually

late manifestation of hereditary syphilis. This is more than a mere predisposition, and since the probability is that at the time of the begetting of the children the syphilis of the parents "—there is no evidence that the parents had syphilis—" had disappeared, or almost disappeared, it follows that its effect on the offspring is delayed, and not characteristic; it appears more as a special form of disease to which the syphilis bears only a remote relation."

Apparently Homén feels that the disease ought to be considered a parasyphilitic condition, although he does not actually use the expression, for he refers both to tabes and general paralysis in this connexion—viz., that of the remote action of syphilis.

These speculations of the older writers on the subject serve to emphasize the obscurity that surrounds the disease. To-day, however, there are no fewer than twelve cases (ten of which came to autopsy) to which we may turn for an independent consideration of the clinical and pathological data they furnish, and we are in a better position to appreciate the importance of certain factors. There is sufficient material at our disposal to warrant the assertion that where so definite a morbid entity is concerned some conception of the nature and pathogenesis of the disease must be forthcoming. Modern tests and methods of examination, moreover, provide considerable assistance.

(1) It seems certain that the Disease is not due to a Congenital or Abiotrophic Defect.

Homén himself has remarked on the normal physical growth and mental development of his patients, previous to the onset of the disease. I have the evidence of the mother of the M. family, that this is true, also, of the three members of her family who eventually succumbed to it. Neither in Ormerod's nor in my own cases was any stigma of degeneration discoverable, or any mental or physical defect noted as rendering the children in any way different from their fellows. On the contrary, they all promised exceedingly well. Four of the five female cases had normally established catamenia previous to the onset of the disease. The evidence against the suggestion appears so conclusive that it is superfluous to elaborate the point.

(2) The Presumption therefore is strong that the Disease is Acquired.

Although a majority of the cases are familial, the fact ought not to be overlooked that in the T. family the sole member affected was

the eighth child, whose case turned out to be, nevertheless, one of the most typical of all (my Case 1). Similarly, in the To. family only one member was affected. There is therefore nothing *essentially* familial about the disease, in spite of the frequent occurrence of familial cases. Nor has any congenital or hereditary instance of the disease been reported. Further, the acuteness of the malady (in some cases) is unlike any congenital or hereditary affection, and the fact that it occurs always in young people brings it into line with more than one well-known toxi-infective condition which has a predilection for youth. These points are in favour of the disease being one that is acquired. The only difficulty, in regard to the familial element, is that sometimes members of a family are affected at long intervals of time one from the other. Thus in my Case 5 the illness began some seven years before it appeared in the patient's brother and sister; they were 3 and 6 years old respectively at the time. Again, five years elapsed between the appearance of the disease in Homén's case W. K., and his case A. K. There is no simultaneous affection of several members of a family, as in such toxi-infective conditions as poliomyelitis, so that it may be debated whether there is not an inherited tendency to the disease, as it may appear at long intervals in the same family. In this connexion it might be instructive to attempt to discover whether in these familial cases the patients who suffered were placed in circumstances different from their brothers or sisters, or were in any way exposed to risks which the others did not run. In my own cases I have not been able to glean any information that is germane to this subject. The matter must be left for the present, until subsequent investigation throws more light on the exact nature of the morbid agent.

(3) THERE IS EVIDENCE TO SHOW THAT THE DISEASE IS TOXIC IN ORIGIN, BUT NONE TO SUGGEST THAT THIS TOXIN IS SYPHILITIC.

The arguments on which this statement is based are of two sorts: those which may be advanced from a study of the acute cases, and those which analysis of certain features of my own cases leads me to offer.

(*a*) All the acute cases are more than twenty years old, and we must be content with a scrutiny of the old records.

Now, in Gowers's and Ormerod's cases, the duration of which was six, thirteen and four months respectively, it is clear we are dealing with an acute illness, steadily and rapidly progressive, associated with high, irregular fever, and with profound disturbances of general meta-

bolism; the symptoms vary from week to week, yet no definite improvement is recorded; from being plump, healthy, intelligent children the patients are speedily reduced mentally almost to the level of "imbecility," and physically to "skin and bone," an expression which cannot be said to be exaggerated—and all within the space of a few months. No morbid process, I submit, can be conceived so widespread in its action and so fatal in its incidence as this, other than a toxic or toxi-infective process.

(*b*) Certain facts in my own cases suggest a toxic origin for the disease.

The clinical history of E. P. (Case 3) is important in this respect. His illness began rather suddenly and unexpectedly, with certain mental symptoms, viz., motor excitement, disorientation, auditory hallucinations, &c.—symptoms which are indicative of a toxic psychosis. In other words, they are the symptoms commonly appearing when the cerebral cortex is thrown out of gear as the result of toxic action, whatever that toxin be and whatever its origin. From this typical toxic psychosis the patient made a good recovery, yet within a few months of his discharge from the hospital the physical symptoms of progressive lenticular degeneration made their appearance. This fact is at least suggestive of the continuance of the action of some toxin on the nervous system.

Again, the transient mental symptoms from which his sister suffered in the early part of her illness, as distinct from the general mental deterioration—such as it is—which some patients with progressive lenticular degeneration show, suggest an intoxication of some sort. I do not think the argument is invalidated by the objection that in neither case were these symptoms persistent. Considering the variability of action of toxins, and the fact that a part of the brain other than the cortex is more profoundly affected, so that other nervous symptoms are more in the clinical picture, it is not remarkable that this should be so.

(*c*) The variability of many of the symptoms from time to time suggests a "functional" or "nutritional" rather than a structural change.

Gowers, Ormerod, Homén, and myself have in turn been struck by the odd way in which the patients, seemingly so inarticulate, have occasionally been able to utter words or phrases with comparative ease and distinctness. Similarly, notwithstanding their appearance of helplessness, in the early stages of the disease their voluntary movements and their muscular control and power have so varied from time to time that the suspicion has crossed the mind of more than one

observer that the condition was "functional." This being so, and in the absence of so-called "organic" signs, it is natural to suppose that some morbid agent is at work producing varying disturbances of function while structural change is as yet slight, and no agent is more likely to produce that form of disturbance than some form of toxin, autogenous or otherwise.

As for the question of this toxin being syphilitic, the whole weight of the pathological evidence in my cases is against that hypothesis, even if we ignore the fact that clinically there is no more reason why syphilis should be proposed as a possible explanation of the disease than, say, malaria. There is no single pathological lesion in my cases, of vessels or meninges or viscera, which resembles what is found in syphilitic disease of these structures. In none of the old or the recent cases is the liver condition identical with, or suggestive of, a congenital syphilitic liver. Further, the pathological evidence of Homén's cases cannot, in my opinion, be taken to support a syphilitic hypothesis. The remarks already quoted from Homén show his own theory to be that the disease is parasyphilitic, *faute de mieux*. Finally, although acute syphilitic meningitis is a recognized clinical and pathological entity, it is nosologically irrational to conceive of syphilis hereditaria tarda causing an acute and rapidly fatal illness—in a few months—after years of normal, healthy, mental and physical development.

(4) It is possible this Toxin may be Elaborated in the Liver.

Cirrhosis of the liver is an absolutely constant feature of the disease, and the opinion therefore is not unwarranted that it must be integrally associated with the pathogenesis of the condition, the more so because it is the sole visceral change which is always found *post-mortem*. The question remains: Is the cirrhosis primary, and the lenticular degeneration secondary, or are both the effect of the action of some morbid agent? We have already seen reason to believe that the disease is of toxic origin. The problem, then, may be stated in another way: Is a toxin liberated or elaborated in the liver which has a double action, on the liver itself and on certain nervous tissues? Or is it produced elsewhere, and has it a simultaneous incidence on the liver, producing cirrhosis, and on the lenticular nucleus, causing the latter to degenerate? Or does some morbid process act on the liver, which is thus made to produce a poison that affects the corpus striatum? How does the presumed toxin act, and what is its nature?

It is obvious, of course, that such questions are more easily posed than answered. One or two points, however, may be alluded to.

While all previous writers on the subject have remarked on the absence of hepatic symptoms during life—in this connexion the loss of appetite and occasional vomiting of Homén's patients cannot be regarded as specific—there are three cases in the series in which certain liver symptoms were present at one time or another, and it is to these that attention must now be drawn.

At the age of 21, S. T., my Case 1, had an attack of jaundice of five weeks' duration, and for several years thereafter she showed at intervals definite signs of persisting liver disease in the form more particularly of œdema of the legs and feet. Four years after this attack, and at a time when the liver disease could not have been long in abeyance, the earliest symptoms of progressive lenticular degeneration made their appearance, in the shape of bilateral tremor. Such a sequence of events is very suggestive, although I admit, as far as the series goes, it is all but unique. It may be taken to show that where liver symptoms are present at all they antedate the lenticular symptoms. Similarly, M. To., my Case 4, had a definite attack of jaundice, of about three weeks' duration, some three and a half years before the onset of the lenticular symptoms. In her case the jaundice cleared up without leaving any "reminder" of hepatic mischief, in the shape of œdema or otherwise. Nevertheless the association is important, and the same deduction may be made from this case as in Case 1—viz., that if liver symptoms occur they precede the nervous symptoms.

C. J., my Case 5, had unmistakeable liver symptoms during life in the form of ascites and œdema, and in this respect the case is unique; none of the others has presented the combination of liver and of lenticular symptoms at one and the same time. From the clinical record, it would appear that the two ran a course *pari passu*. What importance to attach to these facts it is difficult to determine. Cases both more acute and more chronic than this one have not shown any liver symptoms at all. There may have been some pathological complication which produced them in the case of C. J.

If we suppose the condition to be of toxic origin, we have to account for the continued action of the morbid agent, as it is unlikely that once lenticular degeneration commences it must inevitably proceed without further aggravation. Now, when it is remembered that the disease of the liver—a hepatitis with resultant cirrhosis—is a universal feature, that it is always advanced, even in the

acute cases, and that no other viscus shows a constant change, it is natural to suggest that this disease has much to do with the continuance of action of the toxin. Further, the microscopical evidence furnished by examination of the liver proves that the changes in it are always active, for necrosis and regeneration proceed side by side. This may, I think, be taken to suggest that the morbid process is never in abeyance, as far as the liver is concerned, and that fresh areas of that organ are attacked while others recuperate. On the other hand, as Homén's and my own cases conclusively demonstrate, the longer the duration of the disease the greater the disintegration of the lenticular nucleus. Hence we are justified in advancing the hypothesis that the disease of the liver is in some way the cause of the lenticular disease.

While perhaps it may be a little difficult to conceive of toxic action as prolonged as one or two of the cases are presumed to show, it must not be forgotten that between the acute and the chronic cases there is no noteworthy distinction, as far as duration goes. The exact duration of the series of cases, in order of length, is as follows: 4 months, 6 months, 13 months, 2 years, 2½ years, 3 years (two), 4 years, 4½ years, 6 years, 7 years. There is no abrupt interval between the acute and the chronic types. This fact by itself is in accord with the hypothesis here offered.

(5) The Toxin has a Specific Action on the Lenticular Nucleus.

A toxic condition usually suggests a generalized condition, but many toxins have a specific action, instances of which readily suggest themselves. In progressive lenticular degeneration the action of the toxin is both general and local. Among the effects of the former process are the disturbances of metabolism, more particularly in the acute cases, the mental signs of toxæmia, and so on. The local effects of the toxin are seen in the degeneration of the lenticular nucleus on both sides. In this respect my Case 3 is particularly instructive, for in it the disease has not progressed too far; we can see, as it were, degeneration in the making. It is unnecessary to repeat what has often already been noted, that the selective action of the morbid agent is by far the most striking characteristic of the disease—optic thalamus, internal capsule, and caudate nucleus intact, lenticular nucleus shrunken, atrophic, crumbling. It is true, of course, that in Case 1 slight disease of one optic thalamus occurred, and that the external capsule has been involved in more than one case; the caudate also is sometimes rather smaller than normal—*i.e.*, some-

what atrophic. But the contrast between the entire disintegration of the putamen and the conservation of the other ganglia is none the less striking. Let it not be supposed that this selective section is merely a question of vascular distribution. According to the latest and most accurate researches the lenticular nucleus has two, if not three, main sources of vascular supply, distinct from each other. Were we dealing with disease in a particular vascular distribution the structural changes would be quite different. Compared with the cavitation of the right lenticular nucleus (fig. 29) it is remarkable how well preserved are all the tissues round it. It is clear that no mere question of vascular supply will account for the steady disintegration of a collection of grey matter in one place, while other collections of grey matter in close proximity are unaffected. It is in my opinion possible that in the affected areas the degeneration of the vessels—their fragility and thinning or occasional thickening—may be in part secondary to the degeneration round them. This would certainly seem to be the case with some of the vessels round the lenticular cavities in Case 1. Although it is likely that the toxin, whatever it be, acts on the nuclei viâ the blood-stream, there are no signs of changes in the blood-vessels such as accompany thrombotic softening.

How, then, are the phenomena to be explained? Is there a direct chemical or other affinity between the nerve-elements of the lenticular nucleus and the presumed toxin? The fact of the restriction of the pathological process to that nucleus, at least to a far greater extent than in the case of the other basal ganglia, cannot be gainsaid. A good deal of light is thrown on this obscure subject, I believe, by an analogy of an interesting and instructive kind.

Within the last few years four German observers—viz., Beneke [88], Schmorl [91], Esch [89] and Pfannenstiel [90]—have described cases of a rare variety of icterus neonatorum, distinguished as icterus gravis neonatorum. This form of the disease is familial, occurs in the earliest days of life, and is fatal in a very short time, the infants rarely living longer than a week or two. They are acutely jaundiced; every tissue of the body would appear to be bile-stained, so acute is the process. Successive infants in a family may be affected. Now it is a remarkable fact that while the cases do not show any special nervous symptoms during life the distribution of the bile-staining in the cerebrum and central nervous system generally is curiously selective. Seeing that the infants are acutely and universally jaundiced, it is somewhat astonishing to learn, as remarked by all these writers, that in the brain the lenticular nucleus on each side, the corpus Luysii, the cornu Ammonis, the

nucleus dentatus and olives, the sensory nuclei of the medulla and pons, in particular the eighth and tenth (*not* the motor nuclei), are specially singled out and are stained a bright yellow—in the case of the corpus Luysii and the lenticular nucleus an intense yellow—while the cortex cerebri, the caudate and optic thalamus show only a faint tint or none at all.

This "Kernicterus," as the Germans call it, was found by Schmorl six times in 120 cases of icterus neonatorum; it is not, therefore, so exceedingly rare. The lenticular nucleus and corpus Luysii are specifically mentioned by all as being deeply stained, while the caudate nucleus and the optic thalamus escape; in other words, there is here a localized association of a poison, or whatever it is to be called, with particular nerve-cell groups, and this poison circulating in the system is associated with hepatic disease. In these cases there is no evidence of infection of any ordinary type; syphilis can be excluded. This disease, whatever be its origin, occurs in families, is fatal during the first few weeks of life, and is characterized by profound and generalized icterus; yet in the brain certain cell-groups are singled out, others are untouched. It is important to note that this is no mere question of staining of a matrix or interstitial tissue with bile-pigment, for *microscopically the bile-pigment is found in the bodies of the nerve-cells*, and in their immediate neighbourhood masses of pigment may be deposited.

Now in ordinary cases of jaundice in older people, from whatever cause arising, and in the jaundice of congenital bile-duct obliteration, no such selective staining of grey matter has ever been found, as far as I have been able to discover. The conclusion seems clear that familial icterus gravis neonatorum, of the Kernicterus type, is a highly specialized disease where a toxin presumably of hepatic origin exhibits an affinity for the lenticular nucleus and corpus Luysii, in addition to other smaller collections of grey matter, while it leaves the optic thalamus and caudate nucleus untouched, or practically so.

The analogy Kernicterus offers to progressive lenticular degeneration is therefore highly suggestive. I do not wish to overestimate the value of the analogy, however, and in drawing attention to it, and to the possibility of its opening up a new field of research, enough has been said at present.

(6) The Nature of the Toxin is unknown: it is almost certainly not Microbial.

There is no evidence that progressive lenticular degeneration is microbial in origin. Only the modern cases have been examined from

this point of view. In two of my cases there was abundant trace of infection of bacterial type, but there was every reason to suppose, at the same time, that this infection was terminal, and therefore of no pathogenic significance. The third case, although examined just as minutely for signs of bacterial invasion, was negative. Hence the idea that the disease is of microbial origin may be dismissed.

There is much in the disease for which further research is required. Its problems are easier to state than to elucidate. Whether, for instance, there is any connexion between the disease and the condition of the glands of internal secretion is at present obscure. In my Case 3 (the only case examined from this standpoint), the pituitary, thymus, and suprarenal glands were apparently unaltered. On the other hand, the thyroid was undoubtedly the seat of considerable change, the exact import of which I do not know. It will have been noted that in several cases the spleen has been enlarged, but it does not appear to show much definite change microscopically. With the onset of the disease in the female cases, menstruation became irregular and ceased. These are all subjects on which further investigation is needed.

The conclusions which have been come to, as indicated in this chapter, may be expressed as follows:—

Progressive lenticular degeneration, although it has frequently been recorded as occurring in families, is a disease almost certainly acquired, of a toxic or toxi-infective type. There are no grounds for supposing that the toxin is syphilis or parasyphilis. Certain facts suggest that it is elaborated in the liver, and that it acts, presumably via the blood-stream, on the corpus striatum. In icterus gravis neonatorum a poison, presumably of liver origin, has been found to have a specific action on the lenticular nucleus, corpus Luysii, and certain other small collections of intracranial grey matter. The exact nature of the morbid agent in progressive lenticular degeneration is unknown. It is in all probability not microbial. Possibly it is chemical and of the nature of a lipoid.

Chapter VI.—Pathological Physiology of the more Important Symptoms.

The symptoms which stand out conspicuously in the syndrome of progressive lenticular degeneration are involuntary movements, almost always of the tremor variety, muscular hypertonicity and contracture, dysarthria and dysphagia, and a degree of emotionalism, and they may be considered briefly in turn. The first three form a triad which is never wanting in a typical case of the disease.

(1) Involuntary Movements: Tremor.

In at least nine of the twelve cases accepted for purposes of analysis tremor was an early, a prominent, and a progressive symptom; in two others it was not quite so prominent, "clonic and tonic spasms" being specified as the type of involuntary movement present. For practical purposes, however, tremor—a regular rhythmical alternating contraction of muscular groups and their antagonists—is in the foreground of the clinical picture, and its pathogenesis is a matter of considerable interest.

An immense amount of research has been devoted to the question of involuntary movements, of which there are three main varieties, distinguished as athetosis, chorea,[1] and tremor. Many cases of a conflicting nature have been published, no doubt as the result, in part, of difficulty in distinguishing the varieties above mentioned. Yet, as a rule, they can be distinguished readily enough. Athetosis and chorea are involuntary movements of a different type from tremor, and sometimes they cannot be fully separated from each other. On the other hand, though tremor and athetosis occur together, they are, in my opinion, sufficiently distinct to be described apart.

In a consideration of the whole question it is essential to "think anatomically." Confusion becomes worse confounded unless anatomical details receive their due recognition. An independent analysis of a great number of recorded cases of involuntary movement has led me to the conclusion (which is accepted, I believe, by the majority of neurologists) that the anatomical area, in association with lesions of which involuntary movements occur, is more or less definitely limited to the basal ganglia, superior cerebellar peduncles (and possibly cerebellar nuclei), and midbrain. A few cases, selected at random, will support this contention.

Thus, in athetosis, the lesion has been localized (1) in the corpus striatum (Anton [43], Berger [45], Oppenheim and Vogt [40]); (2) in the optic thalamus (Herz [17], Frey [13], S. A. K. Wilson—an unpublished case); (3) in the red nucleus (Halban and Infeld [16]); (4) in the cerebellum (Pineles [29]). The lesion of chorea (posthemiplegic hemichorea) has been localized (1) in the corpus striatum (Schilder [32]); (2) in the superior cerebellar peduncle (Sander [31], Muratow [25]); (3) in the red nucleus (Bonhoeffer [10], Kolisch [21]). Tremor is caused by lesions (1) in the corpus striatum (Rhein and Potts [62], Démange [49], Eisenlohr [50], S. A. K. Wilson); (2) in the red nucleus (Marburg [24], Holmes [18], Van Oordt [27]); (3) in the

[1] By the term "chorea" is meant that type of involuntary movement which, occurring, e.g., after hemiplegia, resembles the movement of Sydenham's chorea more or less closely.

tegmentum (Bristowe [11]); (4) in the optic thalamus (Leyden [23]), &c. Many more examples might be quoted.

Although at first sight the conflicting nature of the evidence may appear far from encouraging, it requires to be examined more closely. Certain facts, it appears to me, stand out as proven and of prime importance.

(*a*) *The pyramidal tracts must not be too severely injured.* If they are, then no involuntary movements occur. With complete paralysis of voluntary movement involuntary movement is never seen. After a stroke, involuntary movements do not set in until volitional power begins to return. This is true both for athetosis and for tremor. More than one case is on record where the involuntary tremor of paralysis agitans has ceased owing to the occurrence of a stroke. Further, I have seen a case of infantile cerebral hemiplegia, with hemi-athetosis, where the patient was subject to Jacksonian fits on the affected side. An exhaustion-paralysis of the ordinary type used to follow these fits, lasting for about twenty minutes. During that time the involuntary movements invariably ceased completely. Such facts are of peculiar significance for my contention.

(*b*) *A lesion of the pyramidal system is not by itself sufficient to produce involuntary movements.* Innumerable cases of hemiplegia occur where involuntary movements are conspicuously absent. There is no case of involuntary movement on record pathologically in which the lesion did not involve, directly or indirectly, certain areas of grey matter at the base of the brain, or in the mid-brain.

(*c*) *The assumption, therefore, is strong that other, extrapyramidal, paths must be injured.* What are these extrapyramidal paths? There are two that concern us in this connexion, one afferent and the other efferent (*vide* fig. 99). The former is the cerebello-rubro-thalamo-cortical path, which is well recognized anatomically: from the nucleus dentatus, viâ the superior cerebellar peduncle, to the nucleus ruber of the opposite side, and thence to the inferior and external division of the optic thalamus, and so to the sensory and motor cortex. There can be no doubt that with lesions of this system certain involuntary movements are prone to occur. The latter is the lenticulo-rubrospinal system, which is perhaps less well known. The nucleus lentiformis is practically independent of the cortex, but has important descending connexions, viâ the ansa lenticularis, with the regio subthalamica, the corpus Luysii, and the nucleus ruber. From the latter the path is continued as the rubro-spinal tract of Monakow, to the anterior horns of the spinal cord.

To lesions of this system I attribute very important symptoms, as will duly appear. It is to be noted that there is a kind of " short-circuit " between the corpus striatum and the optic thalamus.

(*d*) The next point is, *Are the symptoms (involuntary movements) caused by irritation or by destruction of these extrapyramidal paths?* In this connexion the teaching of Hughlings Jackson [19] is of far-reaching significance. It will be remembered he held that positive symptoms could not be *caused* by negative lesions. Hence, as the clinical symptoms which form the present subject of discussion are essentially positive, they cannot be *caused* by destructive lesions. In this way it is possible to exclude destructive lesions (1) of the pyramidal path, and (2) of the extrapyramidal paths as a *cause* of involuntary movement.

But further, irritation, or rather, irritative lesions, of the extrapyramidal paths are not at all likely to provoke involuntary movements. Experimentally, the optic thalamus and corpus striatum are practically inexcitable. The type of nerve-cell of these ganglia is different from that of the excitable motor cortex. Moreover, it is difficult to conceive of a lesion remaining irritative for years, yet we know that involuntary movements may persist indefinitely. Again, excitation of the cortex never produces movements analogous to athetosis, or chorea, or tremor. We are, therefore, forced to the conclusion that—

(*e*) *Destructive lesions of the extrapyramidal paths in some way allow involuntary movements to occur.* As far as athetosis and chorea are concerned it seems to me, a priori, highly improbable that so complex a series of movements as those of athetosis could be produced by irritation of the optic thalamus or corpus striatum. As above remarked, nothing approaching them can be obtained by excitation of these ganglia. It must be concluded, I think, that the movements constituting athetosis are of cortical origin, and that they are in some way the result of structural or functional defects in the cerebello-rubro-thalamo-cortical path. Absence of normal cortico-petal impulses travelling viâ this path allows the movements of athetosis to occur. It is probable that not all lesions of the thalamus or of other stations in the system cause this failure of cortico-petal impulses, but it is clear, I maintain, that on this hypothesis the occurrence of athetosis from lesions at different levels can be reasonably explained, and thus not a few apparently divergent cases are brought into line. The exact area of the cortex to which go the fibres subserving this " inhibitory " function is not known, but there are grounds for believing that the intermedio-

precentral cortex plays a part in the production of the involuntary movements; in any case, the precentral cortex and the pyramidal path must be comparatively intact. If they are thrown out of gear completely the involuntary movements cease. It is possible, further, that certain corpus striatum lesions, as the result of some intimate association by striothalamic fibres, may occasion athetosis.

With tremor, the case is rather different. Experimental data from excitation of the cortex, corpus striatum and optic thalamus are uniformly negative. Karplus and Economo [20], however, have produced tremor by excitation of the nucleus ruber. From clinical and pathological evidence, it is probable that tremor is the result of disturbance of the efferent extrapyramidal path, the lenticulo-rubrospinal, which I have described. My view is that destructive lesions of this path remove a normal "inhibiting," or rather steadying, influence which the corpus striatum exercises on the anterior horn-cell. As a result of this removal, steady innervation of the anterior horn-cell is impaired, and the more the pyramidal path is innervated the more obvious does the tremor become; in other words, it increases with voluntary effort—a characteristic of the tremor in all cases of progressive lenticular degeneration. In accordance with this hypothesis, if the anterior horn-cell is not intact, if the pyramidal cortex or tract is severely injured, the tremor cannot be so obvious. If the pyramidal injury is profound, there can be no tremor.

It is conceivable, however, that the absence of the normal steadying influence of the lenticular nucleus may make itself felt viâ the striothalamic fibres on the external part of the optic thalamus, and so on the intermedio-precentral and precentral cortex. There may thus be a double action of the corpus striatum on pyramidal innervation—viz., directly on the anterior horn-cell and indirectly on the motor cortex. I am not at present prepared to develop this view further; but what has been already said may help to elucidate the pathogenesis of the tremor which is so striking a feature of progressive lenticular degeneration.

It is only in the sense which has been carefully explained above that involuntary movements are "of cortical origin." The position that tremor is caused by cortical irritation (see, for instance, Sharkey's [33] Goulstonian Lectures, 1886) must be abandoned. Homén's contention that tremor is to be regarded as the "Ausdruck einer Corticalreizung" is similarly indefensible. The pathological features of progressive lenticular degeneration lend support to the view which associates tremor with mid-brain and tegmental lesions generally (Holmes, Marburg), but

I have here elaborated a more inclusive hypothesis, which serves to explain certain other recorded cases in addition. I do not consider that the absence of obvious pathological changes in the red nucleus (beyond the increase in parasite glial cells) and Monakow's bundle in my cases of progressive lenticular degeneration, militates against the views here advanced. The gross lenticular disease and the degeneration of the ansa lenticularis are of course obvious; and I consider that defect of the nervous influx from the lenticular nucleus may determine a dynamic modification of the function of the rubro-spinal system without anatomical lesion.

(2) Muscular Rigidity and Contracture.

All of the series of twelve cases showed rigidity and contracture in greater or less degree. Muscular rigidity, therefore, may be taken as one of the cardinal features of the disease. It is necessary, however, to define the expression more accurately. I have used "rigidity" simply as a general term to indicate the condition of the musculature. What is meant, in exact terminology, is a condition of hypertonicity, involving all muscular groups alike. Even when the limbs are put into a position calculated to produce the maximum of relaxation, palpation of the muscles will convince the observer of their hypertonicity. They feel firm and hard, not of course always in marked degree, but nevertheless to an extent that cannot fail to be noticed. Moreover, on impressing passive movements on a given limb, at any joint, more particularly at the proximal joints, the observer will note that when he flexes passively the movement is resisted by the extensor antagonists, and when he extends, by the flexor antagonists. Thus the hypertonus becomes very manifest. Now it is clear that this condition is different from the ordinary spasticity of pyramidal lesions. In a spastic paraplegia it is usually found that when the lower extremities, which are stiffly extended on the bed, are passively flexed at the knees, the calf muscles are not really hypertonic; on the contrary, they are often curiously soft. The apparent stiffness, and the "sticky" gait, are the result of weakness of the flexors, their antagonists being by contrast hyperactive. This is true of the lower limb in many cases of ordinary pyramidal hemiplegia; the circumduction of the limb in walking is occasioned not by rigidity so much as by weakness of the flexors. The hypertonus of the muscles in progressive lenticular degeneration, then, is not the same as that which is met with in lesions of the pyramidal system. It must

not be forgotten, further, that with this remarkable hypertonicity the abdominal reflexes are not abolished, in a pure case, and the plantar response is flexor, while from the pathological standpoint no degeneration can be found in the pyramidal tracts. It may be definitely stated, therefore, that the condition of hypertonus is of extrapyramidal origin.

It is true that the factors governing muscle-tone are somewhat complicated. In the first place, there is no reason to suppose that in the present series of cases the hypertonus of the musculature is of myogenic origin. In my Case 3 the patient was able voluntarily to flex and extend muscles that were definitely hypertonic, long before true contracture set in. Neither clinically nor pathologically was there any evidence that the hypertonus was akin to the myotonia of Thomsen's disease, or of myotonia atrophica, where the sarcoplasm—the extreme motor periphery—is probably the seat of the disease.

Secondly, while tonus is a reflex phenomenon associated with integrity of the spinal reflex arc—posterior root, anterior horn-cell, anterior root—yet the pathological evidence of my own cases shows that the spinal cord was normal. In certain cases of syringomyelia a hypertonus of cord origin is seen in certain muscle-groups [69], and after lesions of the anterior cornual cells loss of tone is frequent, but in progressive lenticular degeneration another cause for the variations of tonus must be sought. It has already been pointed out that the hypertonicity is different from the ordinary spasticity of pyramidal lesions, which, according to Charcot and others—though this view is now somewhat discredited—results from rèmoval of the inhibitory influence of an intact pyramidal system on the spinal reflex arc.

Thirdly, the association of the cerebellum with the maintenance of muscle tone is no doubt a close one. Atonia is frequent with cerebellar lesions (Luciani [73], Thomas [76], Babinski [66]), and, on the other hand, cases of cerebellar disease with acquired myotonia have been recorded (Levi[71]). I have seen two patients with so-called cerebellar fits in whom, after the tonic stage was over, there was a profound atonia of the musculature, as though the muscles that had been contracting were literally emptied of tone. But in the disease under consideration cerebellar symptoms are notably wanting, and pathologically the layers of the cerebellar cortex, as well as the cell-content of the nuclei, are apparently normal. Further, no definite anatomical lesion is to be found anywhere on the course of the cerebello-rubro-thalamo-cortical system already referred to, even if we are to assume that interference with its

integrity might be a conceivable cause of hypertonus of the skeletal muscles.

Fourthly, the existence of higher centres which are concerned with the maintenance of tone must be conceded. There is increasing evidence in favour of the view that muscular tonus depends, to some extent at least, on the reaction between the basal ganglia, and between them and the cortex. I do not think that there is any satisfactory evidence to place such tone-centres in the medulla, pons, locus niger, crus, &c. Thus in certain cases of hemiplegia the paralysis may be minimal, while the affected limbs become peculiarly hypertonic, a hypertonicity which involves all muscular groups alike. The condition has been called "hemitonia apoplectica" (Bechterew [67], Pfeiffer [75]), and more than one case has come under my own notice. As far as I am aware no pathological examination in this condition has yet been made, but that the hypertonicity is of central origin is patent. Again, a case has been recorded by Etienne [68], in which a post-hemiplegic "hemi-tonoclonic syndrome" of a striking kind occurred in a woman, aged 49, with a right hemiplegia. There was a severe degree of volitional paralysis of the right side, but the muscles were actually hypertrophied from overaction of an involuntary nature. There were more or less constant attacks of violent hypertonic spasmodic contractions of the muscles on that side, which frequently began by marked involuntary tremor, passing into tonic spasm. Rhythmic clonic tremor of the right leg was almost unceasing. In addition to the ordinary contracture of hemiplegia there was active tonic contracture, coming in "attacks." Etienne employs the phrase, "a permanent muscular erethism." The resemblance between this case and the phenomena described in one or two cases of the acute variety of progressive lenticular degeneration, as well as in one of Homén's cases, is very intimate and instructive. There was no *post-mortem* examination in Etienne's case, but of the central origin of the hypertonicity no doubt can be entertained.

Further, cases of hemiplegia presenting the converse of this are occasionally met with, viz., cases in which the affected limbs remain permanently atonic—apart, that is, from mere paralysis, and in which no contracture develops. The pathology of these cases is apparently unknown.

From all these facts it may reasonably be assumed that there are cerebral centres concerned with the maintenance of tone. It is also, I think, undeniable that symptoms of this kind require the involve-

ment of nerve-cells for their continuance, and cannot be accounted for by simple irritation of pyramidal fibres.[1]

It may be asked at this point whether there is any close association, pathogenically, between the tremor and the hypertonicity. The two phenomena proceed *pari passu* in the disease we are considering, as a rule, and are observed to vary in intensity from time to time, as well as occasionally to come in "attacks." In the majority of cases of tremor which I have seen it is associated with a certain degree of hypertonus of the muscles. Hughlings Jackson used to say that tremor is rigidity "spread out thin," and conversely, that rigidity is tremor "run together." Be this as it may, paralysis agitans is a disease in which muscular rigidity and tremor are intimately linked, and in which, as a rule, the degree of one is in inverse proportion to that of the other. When, therefore, in at least two distinct morbid conditions such an association is found, the suggestion of these two symptoms having a common origin comes within the realms of possibility.

In view of the occurrence of changes in tonus from central disturbances, the suggestion which I make may be expressed as follows: Disease of the corpus striatum, and in particular of the lenticular nucleus, especially if it is bilateral and of sufficient extent, removes a steadying or "inhibitory" influence which that nucleus normally exerts on the corticospinal paths. There is good reason to believe that this influence is exerted either viâ the thalamus on the cortex or viâ the lenticulo-rubrospinal system on the anterior horn-cell. Absence of this "Hemmung" makes the cortical motor-cells react in such a way that one of the results is increase of tonicity of all the muscles reached by the pyramidal tracts. The function of the motor cortex is interfered with to the extent of the development of this hypertonus, with which is coupled motor weakness, but there is no paralysis of innervation. It is probable, further (as explained in a previous section), that absence of a steadying influence on the anterior horn-cell, exerted viâ the red nucleus, is accountable more particularly for the tremor which is so characteristic a feature of the disease, and which is increased by volitional innervation of the corticospinal path.

It may be that variations in the nature of the change of the normal afferent impulses to the sensorium from the optic thalamus will explain the different ways in which the cortex will react—i.e., either by

[1] There is evidence to show that certain lesions of the frontal lobe and of the corpus callosum are connected with the clinical phenomenon of "tonic perseveration" in the opposite limb, but this condition is not of the same nature as the hypertonus under discussion.

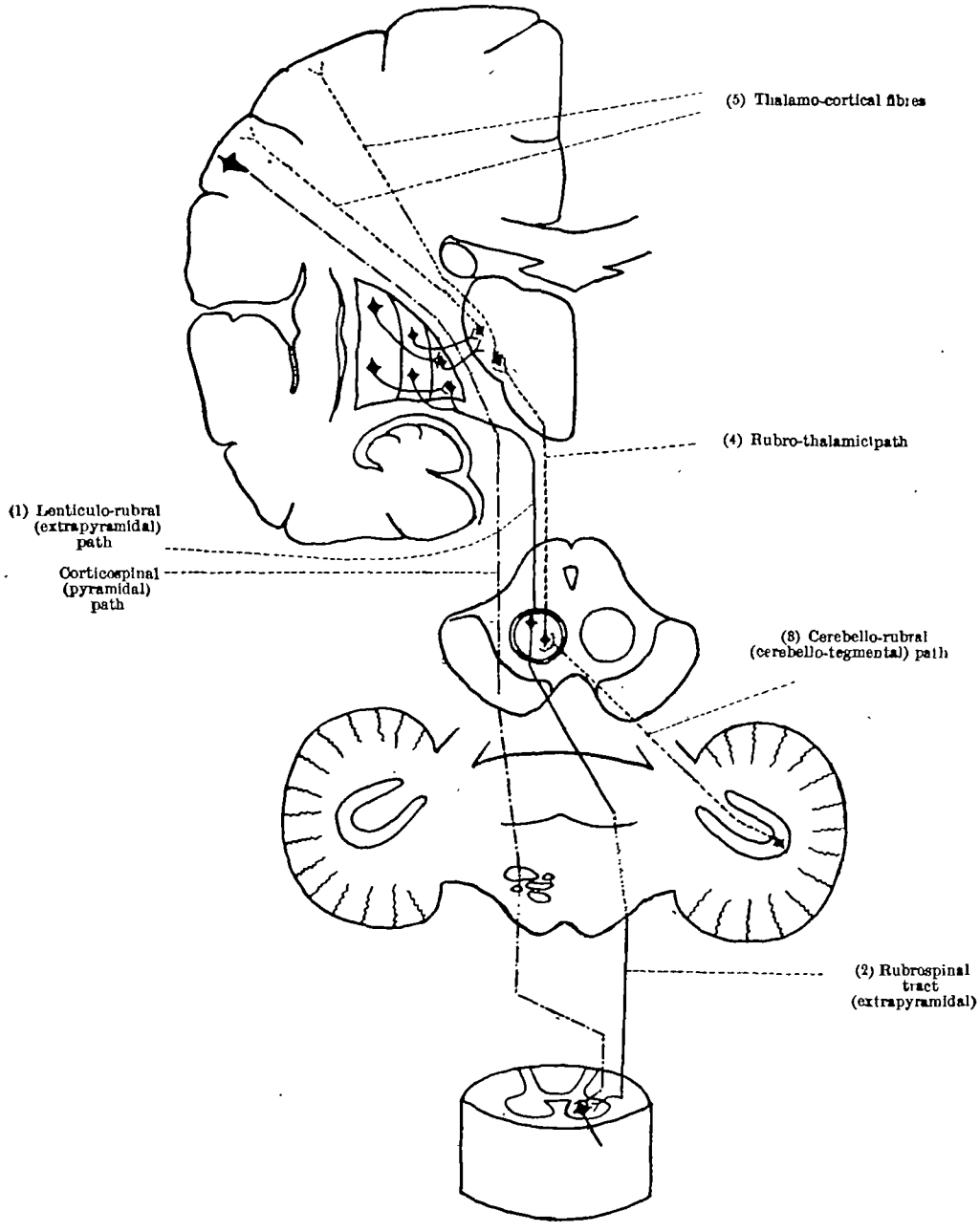

FIG. 99.—Diagram to show the relations of the pyramidal and extrapyramidal systems, and the afferent cerebello-cortical system. (1) and (2) constitute the lenticulo-rubrospinal path (efferent); (3), (4), and (5) the cerebello-rubro-thalamo-cortical path (afferent).

involuntary movements or alterations in myotonus, or both. It seems tolerably clear that interruption of centripetal impulses causes arhythmical and asymmetrical innervations from the cortex, but, as remarked above, in the case of the thalamus the area affected, either directly or indirectly, as a result of which cortical innervation is disturbed, is probably limited. In the case of disease of the lenticular nucleus, such an indirect causation must be postulated, for it has practically no direct connexions with the cortex at all.

Athetosis and chorea differ from tremor in that the former, at least, is in most cases associated with muscular hypotonia (but see [70]). Athetosis, then, is an instance of the coupling of involuntary movement with diminished tonicity, and its pathogenesis, although it follows the lines which have been sketched, must be somewhat different. Wherein this difference consists, anatomically, is in the present state of our knowledge uncertain, but because the involuntary movements and the state of muscular tonus differ from what obtain in progressive lenticular degeneration, the general hypothesis enunciated above is not thereby invalidated.

The occurrence of contractures in extrapyramidal motor disease is noteworthy. With the exception of paralysis agitans, the disease which is here described is the first, apparently, in which contracture has been shown to occur with an intact pyramidal system. It is highly probable that the fixity of the limbs in the contracture-attitudes already described (the result of the absence of impulses from the corpus striatum to the cortex) has facilitated the development, at a subsequent stage, of true contracture. Metabolic changes and the resulting muscular wasting have also, no doubt, much to do with the appearance of this condition.

(3) Dysarthria: Dysphagia.

Dysarthria is the third of the cardinal features of progressive lenticular degeneration. For its pathogenesis two views may be advanced.

Brissaud [77] was the apostle of the theory which placed subsidiary motor centres for articulation and deglutition in the putamen. According to this view, the dysarthria that is so prominent a symptom of pseudobulbar paralysis is not due to implication of capsular fibres, but to involvement of these secondary centres in the putamen, or of the fibres coming from them. Apart, however, from the fact that there is no experimental evidence to support this view, and that there are certain histological difficulties in the way of its

acceptance, the clinico-pathological method has demonstrated its erroneousness. The reader is referred to the researches more particularly of Comte [78] for full discussion of the evidence. Many years previously, however, Ross [63] had come to identical conclusions. In pseudobulbar cases the cause of the dysarthria and dysphagia is involvement of the motor fibres from the lower motor cortex (operculum), somewhere in their course skirting the lenticular nucleus, via the genu of the capsule and the inner section of the crus, to the corresponding nuclei of the medulla.

Now, in my Case 1 it is true that the genu of the capsule is definitely, though slightly, affected on one side. But it is important to note that in Case 3 an equal degree of dysarthria and dysphagia occurred; yet there was complete integrity of the internal capsule and pyramidal tract generally. It is necessary to advance, therefore, another explanation for the production of these symptoms. It seems most natural to associate the dysarthria with the general hypertonicity of the skeletal musculature. The muscles of the throat, palate, and tongue were just as involved in the overaction of the pyramidal system as any of the other muscles of the body. Volitional control over them was just as feeble and imperfect—in fact, the smallness of the movements concerned in articulation is a good reason for the early appearance and profound degree of dysarthria which characterize all the cases. This view, moreover, brings these symptoms into line with certain others. In the clinical histories it will be remembered that several observers, including myself, noted considerable variability in the dysarthria and dysphagia from time to time. Were these symptoms due to structural defects of their innervating neurones, this variability could not, in my opinion, be explained satisfactorily. If it is regarded, however, as due to variable disturbance of a steadying influence, exercised by a large ganglion that is slowly degenerating, the fact of the articulation being better at one time than another is not to be wondered at.

If the disease advances, and the patient lives long enough, it can be readily understood that the "faisceau geniculé" may eventually become affected on one or both sides, in which case the anarthria and dysphagia become those of a true pseudobulbar paralysis. In that case the patient would have definite paralysis of the palate and tongue. It may be mentioned again, however, that in my own cases neither the palate nor the tongue was paralysed in reality, in spite of the profound degree of anarthria. Thus the view of the pathogenesis of these symptoms here advanced is the only one that explains the clinical observations satisfactorily. (See also p. 453.)

(4) Emotionalism.

A degree of emotional overaction, in the shape more particularly of involuntary laughing, is a frequent, though not a constant, feature of the disease. The association of "rire" and "pleurer spasmodique" with disease of the basal ganglia has long been recognized; it is very common in double hemiplegia and pseudobulbar palsy, and occasionally occurs in simple hemiplegia. In my own cases I could not always determine that the involuntary laughing was associated with any definite affective tone; on some occasions, at least, the patients did not appear to experience the emotion which their musculature seemed to express.

The exact relation between the clinical phenomena and the pathological changes—indeed, the exact site of the latter—have not been elucidated with any completeness. Following Nothnagel, it has been commonly taught that involuntary emotionalism occurs in disease more particularly of the optic thalamus; but, assuming this is the case, the pathogenesis of the condition is not thereby made more obvious. In progressive lenticular degeneration the thalamus is not involved directly; there is a notable loss of striothalamic fibres, by which, presumably, some functional interaction of these two ganglia is maintained. The striothalamic fibres go mainly to the outer part of the thalamus, which is the section of that ganglion more definitely connected with the sensory system and with the cerebello-rubro-thalamic system. But it must not be forgotten that involuntary laughing is a positive symptom, and cannot be caused by a negative lesion. It is on a par with the other symptoms indicative of defect of cortical control, and it may be supposed that a sensory stimulus either reaches the cortex via the thalamus, and there produces an unusual effect through impaired pyramidal function, or that by a short-circuit from thalamus to corpus striatum, and so to anterior horn-cell, or rather to its pontine analogue, an uncontrolled innervation of the latter is effected. In any case I do not consider that either optic thalamus or corpus striatum can be regarded as a "lower motor centre" in any sense analogous to the motor cortex; the *only* "lower motor centre," or "subcortical motor centre," which exists is the anterior horn-cell of pontine, bulbar, or medullary grey matter.

Chapter VII.—Syndrome of the Corpus Striatum.

The lenticular nucleus, and corpus striatum generally, occupy a considerable area in the middle third of the cerebral hemispheres; the arrangement of cells and fibres in them is somewhat complicated, and it is contrary to physiological conceptions to suppose that ganglia of such a size should be unimportant from a physiological standpoint. It is, however, undeniable that our knowledge of the functions and pathology of the corpus striatum has hitherto been curiously indefinite. On the one hand, small lesions of that body have often proved to have been entirely without effect, from a symptomatological point of view, and even larger lesions have sometimes, apparently, failed to reveal themselves by any recognizable symptoms during life. On the other hand, uncomplicated involvement of the corpus striatum is a comparative rarity, and the proximity and close relationship of the corticospinal paths have led observers to attribute to impairment of the function of the latter any symptoms which otherwise might have been associated with the lesion in the former region. For these, among other reasons, the prevailing opinion on the physiology of the corpus striatum has been one of uncertainty. Thus Monakow, in the latest edition of his well-known "Gehirnpathologie," is forced to adopt a negative attitude. "In spite of the investigations of numerous experimenters, we know as little of the clinical effects of lesions of the lenticular and caudate nuclei, or as much, as Nothnagel did twenty-five years ago."

In the disease which I propose to designate progressive lenticular degeneration three desiderata are fulfilled on which the establishment of a corpus striatum symptom-complex would seem to depend. The lesions are sufficiently large, in the first place; of sufficiently long duration, in the second place; and in the third they are confined to the ganglion itself. My Case 3 offers a perfect opportunity of differentiating lenticular from corticospinal symptoms. With integrity of the internal capsule and pyramidal paths generally there is bilateral degeneration of the lenticular nucleus, which reveals itself by a train of clinical symptoms amply corroborated by the results of the investigation of a number of other cases, all collected in this paper, so that a general review provides a striking confirmation of the general statement.

The syndrome of the corpus striatum, therefore, which is here put forward, may be expressed as follows:—

In pure, uncomplicated, bilateral lesions of the lenticular nucleus, and more generally of the corpus striatum, provided they are of sufficient

size and of adequate duration, the clinical symptoms are bilateral involuntary movements, practically always of the tremor variety; weakness, spasticity or hypertonicity (sometimes spasmodic contractions) and eventually contracture of the skeletal musculature; dysarthria or anarthria and dysphagia, and a degree of emotionalism; but without any sensory disturbance, without any true paralysis, and without any alteration in the cutaneous reflexes. If the abdominal reflexes are absent (apart from muscular rigidity) or the plantars of extensor type, then the syndrome is no longer pure.

In view of this syndrome, thus differentiated for the first time from a study of progressive lenticular degeneration, the loose way, sometimes adopted, of considering "signs of organic nervous disease" and "signs of pyramidal nervous disease" as one and the same thing must be definitively abandoned. Pure cases of progressive lenticular degeneration show no signs of pyramidal defect of function (as estimated by the reflexes), but the disease is none the less one of the most serious organic diseases of the nervous system that the neurologist is likely to encounter. It is unfortunate that there is no expression in common use to indicate extrapyramidal motor disease.

It has been already remarked that the resemblance between progressive lenticular degeneration and paralysis agitans is considerable. In the latter there is a symptom-complex of tremor, rigidity, and weakness; sometimes there is a degree of emotional overaction, and, as in early cases of the former disease, the patient's utterance is monotonous and sometimes dysarthric; "il a perdu le chanson du langage," to use a picturesque French expression. The articulatory and phonatory defects of the Parkinsonian are in my opinion the result of rigidity of the corresponding musculatures, and not due to a true pseudobulbar condition. Hence the relation between the two conditions is very close, that is to say, as far as the clinical symptoms are concerned, for there are differences of age and etiology and duration which are obvious enough. It might be expected, then, that the pathology of the two conditions, or at least the localization of the lesions, should be more or less identical. Hitherto, in paralysis agitans, no certain pathology has been demonstrated. But within recent years various data have accumulated to show that its lesions will probably be found in the basal ganglia and regio subthalamica. What is paralysis agitans but an extrapyramidal motor disease? Its pathology must therefore be looked for along the lines that have been indicated in the last chapter. In this connexion it is of great interest to note that Jelgersma [87] has found bilateral

degeneration of striothalamic fibres and of the lenticular bundle of Forel in that disease. That investigation in this field will be amply repaid I am firmly convinced. We need not look for gross anatomical lesions in paralysis agitans. It has been pointed out above that dynamic modifications of function may be produced without much anatomical change, and such may well prove to be the case in Parkinson's disease.

The syndrome of the corpus striatum here given differs in some important respects from other corpus striatum syndromes recorded in recent years by different observers, who have based their conclusions on pathological material of somewhat varying nature. At the same time it presents close analogies to one of these, to be referred to immediately, which, in my opinion, is best entitled to consideration.

(1) Piazza [41], basing his conclusions on the case of an old man aged 74, a senile dement, in whom generalized cerebral arteriosclerosis was found *post-mortem*, with bilateral softening of the putamen, as well as on a number of recorded cases, describes a syndrome of the lenticular nucleus, comprising slight paresis, dysarthria, trophic and sensory disturbances. If the middle section of the putamen is involved there is paresis of the limbs; if the lesion is outside this, choreic and athetoid movements may result.

Cases of this description are plainly unsatisfactory from several points of view, and the syndrome itself contains features which cannot be accepted as characteristic of lenticular lesions.

(2) Franceschi [35] describes a lenticular syndrome consisting of forced laughing and crying, dysarthria and double hemiparesis, and assumes that through the lenticular nucleus run the thalamo-cortical paths concerned in emotional expression. In his case, one of bilateral lenticular softening, the anterior limb and genu of the internal capsule were implicated on the right side, and part of the posterior limb on the left side.

Apart from the fact that anatomical evidence is against the assumption just quoted, no case can be considered free from objection where the corticospinal paths are involved as well.

(3) Mingazzini's [39] lenticular syndrome consists of slight facial and limb paresis on the opposite side, exaggeration of the tendon reflexes, anisocoria, sometimes atrophy of the extremities, and slight disturbances of objective sensibility; if the posterior four-fifths of the left lenticular nucleus is involved, then dysarthria or anarthria is superadded. If the outer third of the ganglion is diseased, the "pseudomelia paræsthetica" of Bechterew [44] may occur.

This syndrome, to the inclusion of certain features of which I cannot consent, has been quite recently enunciated by its author. It is based on the study of certain cases of cortical softening, Rolandic and otherwise, where some atrophy of the lenticular nucleus was found on the same side. When the upper and middle thirds of the precentral gyrus are destroyed, as in one of his cases, it is difficult to see how lenticular and corticospinal symptoms can possibly be differentiated.

In an earlier communication, Mingazzini [38], basing his researches on some thirteen cases, claimed that the lenticular nucleus is a motor organ of some kind, that even a small lesion of it never fails to manifest itself by motor disturbances, and that it is subdivided as is the cortical motor zone. He stated that the usual form of motor disturbance is a dissociated paresis or paralysis, sometimes with "irritative" symptoms, as a rule in the shape of tremor. He assumed that there are fibres from the motor speech cortex to the putamen, and from the putamen to the pontine and bulbar motor nuclei.

There are certain difficulties in the way of accepting these views, and the anatomical assumptions are open to criticism. There is, further, no unequivocal evidence that the lenticular nucleus may be subdivided as is the cortical motor zone. Involuntary movements are not produced by "irritation," while true paralysis does not result from disease of the putamen or globus pallidus. Mingazzini does not separate the pyramidal from the extrapyramidal symptoms as I have endeavoured to do, nor does he utilize the cutaneous reflexes as an aid in the matter.

(4) Dana [34] has published some cases of acute gas poisoning, where death has resulted in the course of a very short time. In some of the cases the lenticular nuclei were found *post-mortem* to be the seat of an acute hæmorrhagic softening. From these cases he concludes as follows :—

"The corpus striatum has not any independent or specific motor function. It probably has some supplementary motor function, especially in connexion with articulation. It may have some control over the bladder (double lesions). It seems to have some control over vasomotor and trophic conditions of the skin. It has no thermic centre. It may have some supplementary and associative psychic function, so that lesions affect memory and initiative. In severe gas poisoning there is a double softening of the lenticular nuclei, due to thrombosis of 'the artery of cerebral thrombosis,' and there result vasomotor and gangrenous conditions of the skin, so that these conditions in connexion with a history of coma from gas poisoning form a group of symptoms called 'the syndrome of the corpus striatum.'"

Apart from the indefiniteness of Dana's conclusions, why coma, vasomotor palsy, and gangrene, the result of acute gas poisoning, should be dignified as a "syndrome of the corpus striatum" I am at a loss to understand.

(5) Mills and Spiller [37], from an analysis of some eleven personally observed cases, not a few of which are complicated by other—i.e., extra-lenticular—lesions, find it difficult to form positive conclusions as to the symptomatology of lesions of the lenticular nucleus. They state *inter alia*, that :—

Lesions restricted to the lenticula apparently do not cause sensory symptoms; speaking generally, the nucleus may be regarded as a motor organ; the left nucleus probably contains centres which are concerned with the "movements that make speech possible"; destructive lesions of certain portions of the nucleus probably cause a paresis of the limbs or face, but it differs from that produced by capsular lesions, not being so severe or characteristic.

These authors do not refer to involuntary movements, nor to hypertonicity or rigidity, nor to the condition of the reflexes. "Lenticular centres concerned with the movements which make speech possible" is an ambiguous expression the exact purport of which is not clear.

(6) Oppenheim and Cécile Vogt [40] have described two cases (mother and daughter) of "congenital infantile pseudobulbar paralysis," in one of which a *post-mortem* examination showed a bilateral atrophic marbled condition ("état marbré") of the corpus striatum, including the caudate nucleus, the putamen and the globus pallidus. The internal capsule was intact—was, indeed, rather hypertrophied. The clinical symptoms were spastic contracture of the limbs, dysarthria, choreo-athetoid involuntary movements of the limbs and facial musculature. The muscles of articulation, phonation, deglutition, and mastication were all in a condition of spastic weakness; the eye muscles were normal; saliva escaped from the lips. Freund and Cécile Vogt [36] have also recorded the case of an old woman, aged 77, with somewhat analogous clinical symptoms, dating from the development of a hemiplegia on the right side in infancy, and in this case a similar but less advanced atrophic "marbled condition" of the corpus striatum was found. The latter investigator has also had the opportunity of examining two other cases where the same curious pathological change was discovered.

Basing her conclusions on this material, Madame Vogt [42] has elaborated and published quite recently a syndrome of the corpus

striatum[1] consisting of spasmodic involuntary movements (athetoid), tremors, associated movements, emotionalism, without paralysis or with little paralysis, without sensory changes, and with no impairment of intelligence.

Although the actual pathological condition in these interesting cases is different from that of progressive lenticular degeneration, and although the clinical symptoms are not entirely identical, the localization of the morbid process is the same, and, moreover, the corticospinal paths are apparently intact. Hence the support which these cases furnish to the hypotheses which I have endeavoured to sustain in this paper is particularly gratifying. The syndrome published by Madame Vogt is the first in which the main function of the corpus striatum, as I believe, has been differentiated from that of the pyramidal system, and it corroborates to a considerable extent the views which I have formulated independently during my research on progressive lenticular degeneration. The syndrome which is furnished by that disease presents in its main features close analogies with that of Madame Vogt. We have involuntary movements, spasmodic contractures, dysarthria, emotionalism, without true paralysis, and without sensory changes. My cases, however, do not show associated movements, nor any type of athetosis. These differences are important, for progressive lenticular degeneration is a disease *sui generis*, and is not to be considered a variety of "athétose double." Madame Vogt holds that her syndrome of the corpus striatum is an "athétose double pure," but I am more inclined to associate tremor than athetosis with the syndrome, for reasons already given, and, moreover, progressive lenticular degeneration is in some respects better calculated to exemplify extrapyramidal disease, inasmuch as the abdominal reflexes are preserved and the plantars are flexor, whereas Madame Vogt acknowledges the difficulty, in her athetoid cases, of determining whether the plantar response is flexor or extensor.

That observer does not enter into the question of the pathogenesis of the symptoms, as has here been attempted; in what way the corpus striatum exercises its "inhibition" is not discussed by her; but the harmony between Madame Vogt and myself as to this "inhibitory" action of the corpus striatum, as to the occurrence of involuntary movements in its absence, and as to the preservation of sensibility, is complete. Madame Vogt holds that in the corpus striatum are certain

[1] "Nous en sommes ainsi amenés à construire un syndrôme du corps strié consistant essentiellement en spasmes, plus ou moins accompagnés de mouvements athétosiques, d'oscillations rythmiques, de mouvements associés, de rire et de pleurer spasmodiques, sans (ou presque sans) troubles paralytiques, sans troubles de la sensibilité et sans troubles de l'intelligence: en d'autres termes, une athétose double pure."

"centres," lesions of which will produce a pseudobulbar paralysis, and she therefore finds herself in accordance with Brissaud and others [79] on this matter. I have shown, however, on a previous page, that a spastic anarthria and dysphagia may result from bilateral lenticular disease, closely resembling, but not identical with, a true pseudobulbar paralysis, seeing that the palatal and pharyngeal reflexes are preserved, and that the patient has still the possibility of a certain volitional innervation of the palate, pharynx and tongue. It is not, therefore, necessary to postulate these "centres," which, as has already been pointed out, are for other reasons improbable.

Other writers who have described cases approximating in one way or another to the syndrome furnished by progressive lenticular degenerations may be briefly mentioned.

Anton [43] has described the case of a boy, aged 9, who suffered from chronic choreo-athetoid movements of the limbs and of the face (grimacing, &c.), marked associated movements, dysarthria, and involuntary attitudes of the extremities; in the lower limbs the involuntary movements, according to the author's description, were more of the nature of tremor.[1] *Post-mortem*, bilateral atrophy and disintegration of the putamen were found, possibly of the "état marbré" type; the thalamus and internal capsule were noted as being intact. This case falls more into the category of so-called "athétose double," and presents close resemblances to the cases recently described by Oppenheim, Freund, and Madame Vogt. Anton considers that the involuntary movements are not the direct result of the destructive lesion, but that the latter removes normally acting inhibitory influences on innervation, acting downwards by a supplementary path, presumably on the anterior horn-cell. He thinks that emotional and associated movements are related to disease of the optic thalamus.

Anton's case, however, and those of the other German observers (above referred to) are not entirely identical, for Anton states definitely that the tonus of the muscles in his case was not conspicuously altered ("der Tonus der Muskulatur war nicht merklich verändert"), whereas in the others, especially Oppenheim's, attacks of spasm of long duration were frequent, forcing the limbs into contracture-attitudes, just as in some of my cases. They are alike, however, in the occurrence of associated movement and of athetoid involuntary movements, which do not occur at all in progressive lenticular degeneration. In my

[1] "Die Zehen fast rhythmisch einander entfernt und genähert worden. In der Muskulatur des Beines nahm die Unruhe mitunter den Charakter eines clonischen Erzitterns an."

opinion the tremor which the German cases showed (Anton, Oppenheim), such as it was, ought to be coupled with the lenticular disease rather than the athetosis, the likelihood of whose origin at various levels on the afferent cerebello-thalamo-cortical path has been sufficiently alluded to. The question of dynamic alteration of thalamic function as a result of corpus striatum disease is an important problem, which has not yet been seriously approached. In any case "athétose double" and progressive lenticular degeneration are different diseases and should be kept separate.

Rhein and Potts [62] have published a case of post-apoplectic tremor from symmetrical areas of softening in both lenticular nuclei and external capsules. The tremor—"alternate flexion and extension at the elbow and wrist, the hand being supinated: the movements were almost constant, only ceasing for a time if his attention was distracted"—was present on the right side only. The authors consider that the lesion on the right side may not have been large enough to cause tremor.

Landouzy [57] has recorded a case of right-sided "athetosis" from the age of 2, in a woman aged 32. The right arm was in a typical hemiplegic attitude, and looked to all appearance fixed and contractured, yet all voluntary movements could be performed slowly—"as if with regret"—so that complete extension at all joints was possible. There was no true contracture. In this respect the case bears an intimate relation to my own lenticular cases. The involuntary movements, described as athetosis, were "petits, faibles, lents, mais incessants." The lesion was an old softening of the left lenticular nucleus, enclosing in its centre a calcareous mass of the size of a haricot bean. The internal capsule was untouched.

Démange [49] describes the case of an old man aged 75, with right hemiplegia, and later a progressive left hemiplegia. On the right side was a rhythmical tremor exactly like that of paralysis agitans, and a similar though slighter tremor subsequently developed on the left side. In this case there was a bilateral softening of the lenticular nucleus, and the internal capsule was said not to be involved on either side.

A case has been put on record by Eisenlohr [50], in an old man aged 73, of paralysis of the lower face on both sides, dysarthria, diminution of motor power in the arms, great feebleness of the lower extremities, "which were seized with tremor on any attempt at walking, or on passive movements of them." *Post-mortem* a cystic cavity was found in the anterior part of each corpus striatum.

I am sorry not to have been able to consult the original description

of a case recorded by Löwy [60], where muscular rigidity, like paralysis agitans, but without tremor, followed bilateral softening of the corpus striatum. The title of the paper is suggestive: "Symmetrische Erweichungsherde beider Hemisphären im Kopfe des Nucleus caudatus und in aüsserem Gliede des Linsenkerns, mit Muskelrigidität."

I have gone over a great number of other cases of lesion involving the lenticular nucleus that have been recorded, but from the special point of view of distinguishing pyramidal from extrapyramidal symptoms they are all unsatisfactory. Certain cases appear to be negative (Hutchinson [56], Bramwell [46]); in others the internal capsule is affected, or the lesions are too recent or multiple, or there is generalized arterial disease, or the descriptions, clinically and pathologically, are not given in sufficient detail (Hebold [55], Canfield and Putnam [47], Fuller and Browning [52], Lépine [58], Ross [63], Reichel [61], Berger [45], Schilder [32], van Gehuchten [53], Ferrazini and Paoli [51], Czyhlarz and Marburg [48], Weir Mitchell [65], Grasset [54], &c.).

A number of cases of the ordinary pseudobulbar syndrome, with a more or less definite double hemiplegia, have been recorded. The majority of these have consisted pathologically of a bilateral lesion in the corpus striatum with involvement of the corticospinal paths (Weisenburg [86], Marshall and Jacob [83], &c., &c). Some cases presenting this syndrome have had lesions apparently confined to the corpus striatum (Ross [63], Leresche [82]). In so far as these cases present symptoms analogous to certain of those of progressive lenticular degeneration they are of value; but from the pathological point of view only the method of serial section will suffice to indicate the exact extent of the lesion, and in cases of this description—i.e., where the difficulty is to distinguish between corpus striatum and corticospinal symptoms—the examination must be considered incomplete if this method is not employed. Some of the above cases were not examined microscopically, and the others are unsatisfactory for the reason just given. I have not referred to cases without pathological examination. A clinical case, however, of pseudobulbar palsy occurring in a child (Raymond and Lejonne [84]) may be noted, as in some ways it resembles progressive lenticular degeneration.

Chapter VIII.—Clinical Conclusions.

(1) Progressive lenticular degeneration is a disease of the motor nervous system, occurring in young people and very often familial. It is not congenital or hereditary.

(2) It is progressive and fatal within a varying period; acute cases may last only a few months; one chronic case has as a maximum continued for seven years; the average duration of chronic cases is four years.

(3) It is characterized by a definite symptom-complex, whose chief features are: generalized tremor, dysarthria and dysphagia, muscular rigidity and hypertonicity, emaciation, spasmodic contractions, contractures, emotionalism. There are also certain mental symptoms, either transient and such as one sees in a toxic psychosis, but not severe, or more chronic, consisting in a general restriction of the mental horizon, and a certain facility or docility without delusions or hallucinations, and not necessarily as progressive as the somatic symptoms. The mental symptoms may be very slight and are sometimes absent.

(4) In pure cases the affection constitutes an extrapyramidal motor disease, for the reflexes are normal from the point of view of the function of the pyramidal tracts.

(5) The neurological symptoms constitute a syndrome of the corpus striatum, which has not hitherto been differentiated in this disease.

(6) In some ways the disease bears a resemblance to paralysis agitans, and throws light on the problem of that affection.

(7) Although cirrhosis of the liver is constantly found in this affection, and is an essential feature of it, there are no signs of liver disease during life.

Pathological Conclusions.

(1) The chief pathological feature of the disease is bilateral symmetrical degeneration of the putamen and globus pallidus, in particular the former.

(2) This degeneration is the sequel to the selective operation of some morbid agent on the cells and fibres of the putamen and lenticular nucleus generally. The caudate nucleus is often somewhat atrophic, but never to the same extent, while other large collections of grey matter in the immediate neighbourhood of the lenticular nucleus—e.g., the optic thalamus, which has partially the same blood supply—is not affected at all in a pure case unless it be indirectly, and to a very slight extent.

(3) The morbid agent is probably of the nature of a toxin.

(4) A constant, essential, and in all probability primary feature of the pathology of the disease is cirrhosis of the liver, not syphilitic or alcoholic; it is multilobular or mixed in type, always pronounced, but presenting a varying pathological picture of necrosis, fatty degeneration, and regeneration.

(5) It is probable that the toxin is associated with the hepatic cirrhosis, and may be generated in connexion therewith. An important analogy may be drawn from the occurrence of "Kernikterus" in certain cases of familial icterus gravis neonatorum, where in spite of the universal bile-staining of the tissues of the body certain collections only of grey matter in the brain show a marked affinity for the circulating poison, while others do not. The parts that are stained deeply are in particular the nucleus lenticularis and the corpus Luysii (among others), while the optic thalamus, for instance, is scarcely stained at all.

(6) The pyramidal tracts are intact from Betz-cells to muscles in a pure case; occasionally certain secondary changes occur of limited significance.

(7) Certain secondary degenerations in the subthalamic region, of physiological importance, follow on the lenticular disease.

Physiological Conclusions.

(1) The corpus striatum exercises a steadying effect on the action of the corticospinal system.

(2) This is effected either by the lenticulo-rubrospinal system, or more indirectly viâ the optic thalamus and its cortical connections.

(3) When this influence is impaired pyramidal function is affected in its turn, and is seen in hypertonicity or rigidity, as well as in tremor on voluntary movement.

(4) There is not, however, any paralysis in the strict sense.

(5) The direct connexion of the corpus striatum with the cortex is minimal.

(6) There is no necessity to postulate articulatory "centres" in the putamen or globus pallidus.

(7) Dysarthria may result without any pyramidal involvement of genu fibres, and with intact cranial nuclei, from hypertonicity of the musculature concerned.

(8) Tremor is due more particularly to failure of function of the lenticulo-rubrospinal system.

(9) Hypertonicity or rigidity of the musculature, due to defect of the "inhibitory" action of the corpus striatum, is possibly associated with impairment of impulses from that body viâ the optic thalamus to the cerebral cortex.

APPENDIX.

Cases 1 and 2. Sir WILLIAM GOWERS, *Review of Neurology and Psychiatry*, 1906, vol. iv, p. 249.

Case 3. ORMEROD, *St. Bartholomew's Hospital Reports*, 1890, vol. xxvi, p. 57.

Cases 4, 5, and 6 (abridged). HOMÉN, *Archiv für Psychiatrie*, 1892, vol. xxiv, p. 191.

Case 1.—The patient was a boy, Sydney M., aged 10, who was admitted to the National Hospital for the Paralysed and Epileptic, on October 5, 1886. His father's brother is said to have suffered from a similar affection at the age of 16, and to have recovered after an illness lasting twelve months; a sister of his father also had "St. Vitus's Dance" at the age of 16, which lasted three months; two children of another sister also apparently suffered from some form of chorea and recovered. The patient was the eighth of sixteen children, of whom eleven were dead, one from consumption, the others, it was said, from bronchitis; his eldest brother was in the National Hospital six or seven years before, and died from some form of paralysis at the age of 15. The patient had never suffered from rheumatism. His symptoms began three months before admission, without any exciting cause. Clumsiness with his knife and fork first attracted attention, and the awkwardness in moving the hands gradually increased; spontaneous movement developed and affected the legs as well as the arms.

On admission he was found well nourished. His heart was normal. Constant, slowly changing movements in the limbs and arms at once attracted attention. A contraction of the zygomatic muscles caused a continuous smile, now greater on one side, now on the other. The mouth was usually wide open and the tongue retracted, but sometimes, by an effort, he could slowly protrude it. The open mouth was due to spasm in the depressors of the lower jaw. If told to shut his mouth he pressed the lower jaw up with his hand beneath the chin, and after a moment or two the spasm seemed to give way, and he closed the mouth easily, but in about a minute the spasm came on again and lowered the jaw. The strong retraction of the tongue interfered much with swallowing, because the tongue was pressed up against the hard palate; liquids taken into the mouth ran out again, unless the jaw were raised up; as the jaw began to descend again he was able to flatten his tongue sufficiently to allow the liquid to pass into his throat, but the tongue immediately resumed its rigid position. This process had to be repeated with each mouthful. He seldom tried to speak, but occasionally managed to utter a sentence which could be understood, especially in the morning. The spasm was always less after sleep, and worse as the day went on. He almost constantly made a low whining sound.

The movements of the eyes were normal, but at times the balls were rolled upwards. There was much spasm in the neck muscles, especially at the back, so that the head was almost constantly bent backwards; there was also strong spasm in the sternomastoids. Occasionally, however, when he sat up in bed,

his back and neck were arched forwards so that his head was between his knees.

Both arms presented slowly changing tonic spasm, greater in the left. The forearms were usually pronated; the fingers half flexed at all joints, and the thumb also flexed. From time to time the spasm increased, and then the elbows became strongly extended, the arms adducted at the shoulder. Voluntary movement was interfered with by the spasm to a less extent than might be anticipated; he could take hold of any object with a little difficulty. At times the spasm changed so that the fingers were spasmodically extended; occasionally they were spread out and moved irregularly in a manner resembling athetosis, now and then more quickly, but the constant tonic spasm prevented any actual resemblance to ordinary chorea. It was always increased by an attempt at voluntary movement, even when this could be effected.

In the legs there was similar spasm, also a little greater on the left side. The left foot was in constant strong extension at the ankle, and inverted; the spasm could not be completely overcome by passive force. It varied less than in the arms, but occasionly passed off entirely for a short time. The right foot presented very little spasm, but at times the leg was extended at the hip and knee by spasm, which came on gradually, and slowly passed away. At the hips the spasm occasionally changed to flexion, and the leg, still extended, became flexed on the trunk at the angle of about 60°. The boy was able to walk; the spasm in the left foot generally prevented the left heel from reaching the ground, but now and then relaxation of the calf muscles permitted him to walk naturally. The abdomen was generally retracted by spasm in the abdominal muscles, distinctly greater on the left side.

When the body was spasmodically bent forwards the spine presented one long curve, with a slight lateral deviation in consequence of the stronger action of the muscles on the left side. The knee-jerk could be obtained on each side, but was slight, apparently from the interference of the spasm. There was no foot-clonus. The plantar reflex was slight, the cremasteric active; no abdominal reflex could be elicited. Mechanical irritability of the nerves was repeatedly searched for in the limbs, but could not be found. Sensation was everywhere normal. He complained of some pain in the dorsum of the left foot. His optic discs were normal. His mind seemed unaffected. When the spasm in the tongue prevented his speaking he would write down the word he wanted to say, and evidently understood everything that was said to him. His urine was normal, and so, at first, was his temperature. When he was asleep the spasm passed away entirely, except in the calf muscles of the left leg; the mouth was closed.

During the first few days after admission a distinct improvement occurred, but after the first week he became rapidly worse. His temperature rose to 100° and 101° F. The spasm had the same character but was greater, and became as severe on the right side as on the left. He ceased to speak intelligibly and became drowsy, and began to pass his urine and stools into the bed.

On October 16 attacks of spasmodic difficulty of breathing came on.

When lying moderately quiet, with the usual spasm of the arms and hands, this would suddenly increase; the mouth opened so widely that the jaw seemed subluxated, and went back with a snap when the mouth closed. As the jaw descended the breathing became quicker, and it was seen that the tongue seemed to be drawn up almost into the throat, so as to impede the breathing, until relieved by drawing the tongue forward and forcibly closing the jaw. During the attack the face was flushed but not livid. Such an attack, lasting half a minute, would recur every four or five minutes. His temperature rose to 101·6° F. and his pulse to 168. The attacks ceased on the application of a spinal ice-bag. Next day he was much quieter, the pulse fell, but the temperature rose to 102·6° F. In the evening the spasms became very violent.

For the next fortnight the condition continued nearly the same, in spite of varied treatment. The temperature continued between 100° and 102° F. and he rapidly lost flesh. Severe paroxysms occurred, in which his respirations were 60 to 80 a minute. The general spasm continued the same in general character, but that in the hands became very uniform. Both were generally strongly flexed at the wrist, the fingers semiflexed, but not forced into the palm, the thumb adducted, the forearm supinated to its full degree, so that the back of the hand was downwards. The face presented little spasm, except during the paroxysmal increase, when his features were distorted. These attacks did not seem to involve the legs, but the extreme extension of the feet continued. The spasm no longer ceased during sleep, but continued much as when he was awake; it seemed to cause little suffering.

A month after admission some improvement occurred: he became able to speak a little. The temperature was generally about 100° F. Emaciation continued; the muscles wasted, but presented no change of electrical or mechanical excitability. In the middle of November there was again an increase in the spasm. The feet were strongly extended at the ankles and the toes were strongly flexed. The spasm of the trunk was still flexor; the body bent forwards, and the thighs flexed at the hip, raising the legs off the bed, so that the patient seemed balanced on the gluteal region. But after two weeks the spasm again lessened, and such flexion of the trunk became rare, but the plantar flexion of the feet and toes increased, so that the sole became arched. The spasm in the arms continued, but the flexion of the left wrist became less than that of the right. During November the temperature varied, sometimes normal for a day or two, then rising to 102°, 103° or 104° F. The wasting steadily increased, so that the child was reduced "almost to a skeleton," although a fair amount of nourishment was taken. During the first fortnight of December the spasm was definitely less, and the temperature was lower, varying from a little below to a little above normal. Occasionally he would talk a little. On December 17 his cheeks and supramaxillary regions were found to be swollen and crepitated on pressure, evidently from air in the cellular tissue. This condition spread down the left side of the neck to the left axilla and left side of the chest, but rapidly lessened in the next few days. The evening temperature was generally 100° or 101° F. The boy became weaker,

ceased to swallow, mucus accumulated in the chest. On December 22 the temperature rose to 104° F., and he died eleven weeks after admission and about six months after the commencement of the symptoms. Throughout, his heart presented no murmur and the urine no albumen. The position of the legs and arms produced by the spasm during life continued after death.

A careful *post-mortem* examination was made, and a thorough naked-eye examination of the brain, spinal cord, and membranes revealed nothing abnormal. The heart was healthy. The cellular tissue of the anterior mediastinum contained air, which extended in front of the trachea and down to the subpleural tissue of the left lung near its root, whence it had evidently escaped. The liver was noted to be "firm, hard, lobular, light in colour, not greasy, and not staining with iodine." (It was evidently cirrhosed, although the significance of this was not realized at the time.) There had been no jaundice.

Portions of the cortex of the brain, of the spinal cord, peripheral nerves and muscles, were hardened and examined microscopically by Dr. Wilson, but no deviation from the normal could be discovered.

Case 2.—Two years later, August 29, 1888, the boy's sister, Charlotte M., aged 15, was admitted, because for nine months she had been restless and lethargic, with some thickness of speech and tendency for saliva to flow from the mouth. At the onset the catamenia, established for eighteen months, had ceased. She was a heavy-looking girl, with mouth generally open and lower lip hanging down, easily excited to laughter. The tongue was rather large, and when protruded had a slight tremulous movement. There was nothing abnormal in the throat except some congestion. She was able to walk well; the knee-jerks were normal; there was no foot-clonus; the optic discs were normal, and no other symptoms were found. At the end of six weeks she was sent to the country branch. But six weeks later "choreic movements" commenced in the right leg, and extended to the other leg and to both arms in a fortnight. She was readmitted on January 2, 1889. The movements increased during the month before admission, and for a few days the legs had been drawn up, flexed at the hip and knee, while her arms were extended and raised above her head. Lying thus there was constant regular movement of the feet, the heels resting on the bed and the toes sharply depressed, and then raised; at the knees and hips there were also slight flexor and extensor movements, moving the heels up and down the bed for an inch or two. Similar rhythmical movements occurred in the arms at the elbows. The trunk muscles and those of the neck and head were free, and the face was still. The tongue now presented no tremor or spasm, and could be voluntarily protruded.

The movements varied in degree, and could be occasionally stopped for a few seconds by voluntary effort. There was no tenderness of the muscles or wasting. Passive movements caused some pain, especially attempts to extend the legs. The knee-jerks could not be obtained (perhaps from the spasm); there was no foot-clonus.

No derangement could be found in any cranial nerve, pupils, eye-move-

ments, or optic discs. The heart was healthy. The urine contained one-sixth albumen (casts are not mentioned). The temperature was raised, and during the first three weeks it frequently reached in the evening 103° or 104° F. She steadily lost flesh and became thinner and more feeble, the movements continued, varying much in degree. At times the forearms were brought in front of the chest, and moved rapidly in flexion and extension.

The only medicine which had a marked effect on the movement was the hydrobromate of hyoscine, but toxic effects prevented its continuance. On the evening of January 23 her temperature was 106·2° F. (verified by several thermometers), reduced to 100° by cold sponging. There was no delirium or headache, the pulse was 180 and respiration 68, although no morbid sign was presented by the lungs. The patient became much more excited, and, apparently in consequence of this, the movements became less violent. The heart-sounds continued normal, but bronchitic râles appeared. The albuminuria continued. Twice again the temperature rose to 106° F. Evacuations were passed into the bed. She died on January 30, the temperature rising just before death to 108·4° F.

Post-mortem examination revealed no morbid appearance in the membranes of the brain; no sign of tubercle could be discerned in them. The white substance of the hemispheres was studded with minute "pits," the size of a pin's head (the significance of which is probably small). No other morbid state could be discovered in the brain. The spinal dura mater was, in places, adherent to the bone, but was not thickened, and presented no other morbid appearance. In the lower dorsal region there was a small extravasation outside the dura mater, but there was no morbid appearance on its inner surface. The spinal cord and sections of this in all parts appeared perfectly normal to the naked eye. The heart was healthy. No sign of tubercle could be found anywhere. In the lungs there was very slight hypostatic congestion.

The liver, of normal size, presented the typical appearance of cirrhosis. Strands of connective tissue enclosed yellow lobules of various sizes rising above the level of the section. The tint was found to be due to fatty and granular degeneration of the cells. The condition of the liver led to careful inquiry regarding alcohol, but it was found she had never taken it. There is no record of a microscopical examination.

Case 3.—Walter William S., aged 10. Admitted to Luke Ward, St. Bartholomew's Hospital, under care of Dr. Gee, September 20, 1889. Transferred to Casualty Ward, October 22, 1889. Died January 21, 1890.

Note on admission.—Three or four months ago right arm and hand noticed to be weak, and fingers to be kept in cramped position. Speech affected soon after arm; could not pronounce his words intelligibly. Speech got a good deal worse about a month ago; has since been scarcely able to speak at all. Not walked quite naturally for two or three months, but this has got much worse during the last fortnight. No difference noticed in the two legs. For about the same time the left arm and hand have "not been right." No trouble with

micturition or defæcation. Some drawing of the face has been noticed from the beginning, but only occasionally, and usually to the left. No squint. Has seemed silly (laughing unnecessarily, &c.) for a month or two. Never had fits.

For about a month has had some difficulty in swallowing; food does not come back through nose, but returns through mouth. Lately saliva has run from mouth. During three or four months some bleeding from ears and mouth; never pus; never headache or giddiness. No vomiting.

Always fairly healthy; got on fairly at school, though never very sharp (in second standard).

Three other children in family—these died young; one with "rheumatism of the heart," two with whooping-cough and fits.

Mother dead; had one or two miscarriages. No family history of consumption or insanity. Maternal uncle subject to fits. A further note, October 31, states: He comes of a neurotic stock. His father frequently weeps; his aunt is said to have had the shaking palsy, and to have recovered from it after eighteen months.

Present condition.—Has rather an idiotic look.

Eyes.—Pupils widely dilated, act well to light and accommodation. Movement of eyeballs good in every direction; no squint or nystagmus. Sight appears good; optic discs natural.

Ears.—Some dried blood in each; no deafness, perosseous or otherwise.

Face.—No very manifest paralysis. Eyes can be closed tightly. On laughing both sides of face move well. Mouth is kept open; it is sometimes drawn a little to right, sometimes to left. He can open it widely; the jaw muscles can be felt to contract well on closing it.

Tongue.—Furred; protrudes it a little way only beyond lips; irregular movements as he does so.

No power of *speech;* cannot say "yes" or "no," but makes the same sound whatever he tries to say.

Throat.—Natural; normal movement of soft palate.

Arms.—No actual paralysis of either arm. Right thumb is kept more or less flexed into palm; is unable to close fist without first drawing out thumb with other hand. Grasp of right weaker than left. Slight rigidity sometimes at wrist and elbow; no increased reflexes. No manifest wasting anywhere, but perhaps a little about thenar eminence. All movements of hands and arms performed fairly, but he cannot pick up pin with right hand. No anæsthesia.

Legs.—Perhaps some rigidity at knees; knee-jerks marked, + right; no ankle-clonus.

Gait.—Rather uncertain and stiff; stands well with feet together and eyes shut.

Pulse 80, good strength. *Respiration* quiet. *Temperature* normal.

Chest.—Heart and lungs normal. *Abdomen* normal; skin reflexes marked.

Spine.—No tenderness or curvature of spine.

Mental condition is perfectly clear; does everything he is told at once.

September 21.—*Urine*, alkaline, 1·014; no albumen or sugar.

September 22.—As to swallowing, nothing very remarkable has been noticed; he eats and swallows mince without any difficulty; he moves his lips well. In drinking he has rather more difficulty, letting the fluid come back from mouth into cup; chokes a little sometimes. Feeds himself quite well; spoon held in right hand, but very awkwardly.

September 23.—Electrical reactions quite natural.

September 24.—Right tympanic membrane seen; looks natural.

September 25.—He can write his name (a specimen appears in the original notes). Nothing can be said about it except that it is clumsy, the letters of different sizes and the upstrokes a little shaky; sometimes will mention a letter pointed out to him, but never pronounces them distinctly; evidently knows the letter well. Sometimes asks for what he wants.

September 26.—Spoke distinctly this morning; referring to his medicine, said "That is water"; but when asked to say anything does not seem able to.

September 29.—Always talks best first thing in the morning.

October 3.—Last night left side of face was much drawn down. Can protrude tongue better. Cannot use hands at all, but is willing to try.

October 11.—Is now frequently suffering severe paroxysms of pain in the left hand. The contractions are then more rigid.

October 15.—Every day has attacks of pain in left hand, and shrieks; lower part of face (not upper) drawn to left. Seems more placid when asleep, and can draw down the mouth at will. Left hand continues flexed and in a condition like tetany, even when asleep. Can talk plainly sometimes.

October 22.—Very noisy and quite a nuisance (had to be transferred to Casualty). Behaves in an idiotic manner. Is able to relax his facial muscles at will.

October 31.—His condition is investigated and described as follows: Thin and emaciated. Pupils dilated; fundi natural. Mouth drawn to left; left side of nose drawn down, and left nostril dilated, but these distortions seem to be voluntary. Can protrude tongue but not at once, and creates some trouble over it. Is unable to talk. Does not seem to be paralysed at all. Left arm is kept contracted at elbow; straightened when he likes. Left wrist and fingers flexed; can also be straightened. Right arm and hand fairly normal, but some approximation of thumb to palm. Prefers to lie with his thighs and knees flexed and feet *en griffe*. But on the application of the needle will put every joint in its ordinary position. Muscles react well to faradism; no R. D. Can walk when he chooses. When he falls about he bruises himself, but not seriously.

November 3.—His temperature, hitherto normal, rises (*vide* chart, fig. 8).

November 4.—Last night had a hot bath; with a view of seeing what he really could do, he was allowed to go under the water. He seemed to realize his position, but made no effort to help himself; swallowed enough warm water to make him sick. Sweated much after the warm bath. Thirsty and feverish this morning. Pain in belly over region of liver.

November 5.—Bit his lower lip slightly. Tongue dry and coated with blood.

November 7.—Dr. Gee can find no signs of local disease to explain the fever. Ophthalmic examination gave no results. After examination he lay and yelled lustily. 4 p.m. sweating profusely. Looks as idiotic as ever.

November 8.—Profuse sweats. Heart-beats 226. Respiration 40. Temperature fluctuates, *vide* chart (rose to 103·6° F. to-day). Takes food well.

November 9.—Improvement. Anæsthetic given and splints applied to straighten the legs; respiration became slower and more regular under the anæsthetic.

November 10.—Left arm much better, uses it volitionally, but right hand appears to be gradually taking on the same characteristics as left; the thumb is adducted and the fingers are beginning to be flexed. He likes the splints. Distinctly said "No" in answer to a question from the house physician. Has paraldehyde to procure quiet nights.

November 13.—Bed-sore appeared on sacrum since yesterday (the splint has been removed).

November 14.—More feverish again. Much flexion of right little toe. Less flexion of legs. Howls vehemently.

November 16.—Cries when he wants anything, but does not speak. Swallows everything that is given him, but does not masticate. Is quite anæsthetic over the bed-sore.

November 18.—Temperature reached 105° F. to-day. Another bed-sore, character like the last. Urine very offensive, alkaline and phosphatic.

November 21.—Face bluish. Still lies drawn up. Never asks for anything. Still yells.

November 22.—Fever abated (*vide* chart); and seems better, excepting the bed-sore, which is worse. Marked spasm of right facial muscles when he attempts to speak.

November 23.—Less rigidity of arms, legs still contracted; looks more cheerful. The improvement seems to have been maintained till December 7, when the constant yelling recommenced. Still lies in fantastic attitude. Understands, but cannot formulate words.

December 10.—Howls dismally about sixteen out of the twenty-four hours. Takes food well, can appreciate when his mealtimes come, but does not speak. Fundus of eyes rather hazy. Bed-sore better. As to the contractions, knees flexed, feet extended. Face now drawn to right, constant movement of right facial muscles.

December 13.—Hard places on lower lip and left cheek, apparently where rubbed by the teeth.

December 30.—Temperature, which has lately been nearly normal, begins to mount again in an irregular fashion (*vide* chart).

January 1, 1890.—His condition is again described thus: He has no appreciation of time or season now; the only thing he can do, and that not humanly, is to devour food ravenously when put into his mouth; he does not chew it,

and is therefore fed on slops. His posture is as follows: Knees drawn up one on either side of chin, so that thighs are flexed on abdomen, and legs on thighs. Feet extended and toes flexed. Left arm flexed to a right angle at elbow, forearm across chest. Left hand flexed at wrist, thumb adducted, and finger adducted and flexed. Right arm generally extended by side, forearms pronated as far as possible; thumb adducted, fingers adducted and a little flexed. In this position he lies, usually howling dismally, so that a half-grain of morphia is given daily. The perverted action of his muscles is intensified, and on the slightest forcible action clonic spasms can be produced. His right eye works now, and the right side of his face. His mouth is not sore, but he has neither the volition nor the power to put out his tongue. He passes everything under him. He sweats profusely. Fundus of eyes natural. Electric reactions natural.

January 15.—The fever, which had abated somewhat since the 4th, is again increasing. Breathes very rapidly. Does not howl so much, sleep induced by morphia. But is in a most deplorable condition; passing everything under him, and lying like a log unless turned over. Bed-sore healed.

January 19.—Much worse, breathes very infrequently, usually four times to the minute.

January 21.—Died.

I made the *post-mortem* the day after his death. The following is a record from the *post-mortem* book:—

External appearances.—Extreme emaciation. Bed-sores on sacrum, trochanter and right elbow. Legs tightly flexed upon his hips, and hips on thighs; they could not be straightened out.

Head.—Cranial bones very thin. Dura mater and sinuses normal. Arachnoid and pia mater rather watery-looking, otherwise normal. Arteries normal at the base. Brain: convolutions perfectly normal in appearance and to touch. Spinal cord normal to naked eye.

The brain and cord were put in spirit and water till next day.

Eye and ear.—Not examined.

Neck.—Not examined.

Chest.—Lungs dirty and flabby-looking, and smelling badly, but no definite disease.

Heart.—Normal.

Aorta and vessels.—Normal.

Abdomen.—Peritoneum normal. Stomach normal. Intestines discoloured. Liver in an extreme state of cirrhosis, weight 16 oz. In size, uniformly small. Surface covered with small rounded elevations. Section firm, and showing bands of connective tissue, enclosing degenerating lobules. Some few of these lobules were yellowish, and so disintegrated that they could be pressed out of the section. General colour of the organ a sort of pinkish-brown.

It was sent to the Museum as a specimen of typical hob-nailed liver in a child.

(In order to meet the wishes of the friends, the examination was to a

certain degree limited, so that the nerves of the limbs were not removed, nor the joints opened.)

Vertical sections were made through the brain next day. In a section at the level of the optic commissure (practically equivalent to the frontal section of Pitres) a small patch of softening was noticed, having the shape and position indicated in the diagram (see p. 310)—i.e., involving the outer layer of the left lenticular nucleus. On a section about 1½ in. farther forward (pediculo-frontal) and on the next section behind (viz., through anterior border of pons = parietal section), this softened patch could no longer be seen. Dr. Gee examined the sections after they had been two days in Müller's fluid. He noticed another similar but smaller streak, symmetrically placed upon the right side. He pointed out that these alone could not explain the whole of the symptoms.

The brain, pons, medulla, and cord were hardened in Müller's fluid, and then further examined. The streak of disease by the left lenticular nucleus was then found to extend backwards and forwards for about an inch, tailing off and gradually disappearing within these limits, but preserving the same position in relation to the adjacent parts of the brain. Thus it formed a small flat area, covering a considerable part of the external aspect of the nucleus, between this and the claustrum. The tract of disease on the right side was in every way symmetrical to the left, except that it was smaller in extent. Microscopically these tracts of disease were found to consist of closely packed lymphoid cells, in which a few vessels ran. They were, I presume, inflammatory.

In the upper part of the pons were some tiny patches, apparently of softening, placed as follows:—

(1) In a section just below the superficial origin of the fourth nerve were two narrow patches, one on each side of the mesial raphe about ¼ in. from it. They were in the dorsal part of the transverse fibres of the pons, lying in the direction of these transverse fibres, and measuring at most ⅛ in. in length.

(2) In a section about half-way between the superficial origins of the fourth and fifth nerves were two little patches corresponding in position to those just described, but smaller; and two other points, the size of pin-heads, lying still more dorsally—i.e., in the fillet.

Microscopical examination was made of many parts of the motor area of the cortex cerebri and of the cortex cerebelli. I could not make out any disease here. The spinal cord also was perfectly normal; there was no trace of descending degeneration to account for the contractures. In the liver was found what was expected from the naked-eye appearances—viz., large bands of connective tissue occupying the periphery of the lobules. In the sections I have, the cells of the lobules are less degenerate than I should have expected. Moreover, amid the connective tissue growth bile-ducts are very numerous and very prominent objects.

Case 4.—Alfred K. was born on December 1, 1866, and was the third member of the family. During his boyhood he had been perfectly healthy, and

not suffered in any way. At the age of 20 he was working as a carpenter. Not long thereafter, in the spring of 1887, he began to suffer from headache and general listlessness, and about the same time his mother noticed that he seemed to become more "simple," and in a general way to "fail" (expression of his mother). At the same time his memory became impaired, but at this time no other symptoms were present.

After about a year of this or rather less, during which time the symptoms were slowly increasing, the patient began to walk in an irregular and uncertain fashion. He also complained of occasional pains in his legs.

At the beginning of 1888, that is to say, about a year after the onset of the illness, he began to have difficulty in articulation. At the same time, or perhaps a little later, a certain stiffness of the whole body was noticed, especially in the lower extremities, which began to contract slightly at the knees and hips. Slight but definite tremor made its appearance in the arms and hands, and gradually increased. All these symptoms gradually became more intense, with the result that the patient became more and more helpless. Occasionally there was vomiting. From December, 1888, the patient was bedridden, and unable to feed himself.

On May 6, 1889, he came under the observation of Professor Homén, who made the following examination :—

The patient is rather small and delicate-looking, but his nutrition is good. The expression of his face is childish, stupid and half idiotic, and somewhat staring. Speaking generally, he seems to take in what goes on round about him, answers simple questions slowly, as if he were thinking about them, but sometimes he does not respond at all. Speech is slurring and difficult, and restricted to a few words or to a short sentence; on the other hand, he does not miss his letters or make mistakes in his words. Movement of the tongue appears somewhat difficult, but there is no fibrillation. The pupils are of medium size and react to light, although a little slowly. Vision is normal, and the other organs of special sense are also normal.

The customary attitude of the patient is as follows :—

He usually lies on his side with his head drawn a little back, though the neck muscles are not much contracted. When he sits up his head usually moves to and fro in a fine tremor. His mouth is often held open, and there are occasionally slight tremors of the lower jaw. Both arms, especially the left, are somewhat flexed, and cannot be straightened beyond an angle of 150°. At the wrist the left hand can be drawn into a line with the forearm, but cannot be dorsally flexed; the first and second phalanges are flexed to a right angle, the third phalanx is in slight dorsal flexion; the forefinger is not so flexed as the others. It is almost impossible to straighten the other fingers. The thumb is contractured, and its movements are very imperfect. The right hand and its fingers is much less contractured and more movable. Almost always a slight slow tremor of the hand is present, mostly from side to side, but occasionally also rotatory. The forearms when they are held free also show a tremor of alternating flexion and extension.

The lower extremities are also contractured, especially at the knee and hip. The knee cannot be extended beyond 150°. Both legs show very definite tremors, especially when the patient tries to straighten them. These consist of alternating movements of the knees and toes.

The musculature is slightly atrophic. The cutaneous reflexes are "weak"; the tendon reflexes cannot be tested well, because of the contractures. There is no obvious disturbance of sensibility and the electrical reactions of the nerves and muscles are normal. The left hand is so tightly closed that it cannot be opened, but the power of the right grasp is fifteen on the dynamometer. During this test a wide, coarse tremor becomes manifest.

During his stay in the hospital the patient's condition gradually became worse in every respect. His perceptive powers seemed to become more feeble, and during the last weeks he never spoke at all, more apparently from failure of perception than from inability to articulate, since even to the end he could occasionally articulate a few words correctly. As a rule the sounds that escaped from him were more or less unintelligible.

The contractures were intensified, but the tremor became rather less; towards the end it came in attacks, which spread over the whole body and lasted from five to ten minutes. Saliva escaped from the constantly open mouth. During the last few weeks of the patient's life, tonic and clonic attacks of cramp lasting about a minute were sometimes noticed. During his stay in the hospital he had steadily emaciated, and a few slight bed-sores made their appearance. On September 1, 1890, his temperature began to rise, and his tonsils became inflamed and swollen. He gradually sank, and on the evening of September 13, 1890, he died, being scarcely 24 years old.

The *post-mortem* was held the next day, and of the long description which the author gives, the following are the essential points:—

The contractures were extreme. It was quite impossible to straighten the arms and legs. The cranium was thickened. The dura mater was slightly thickened also; the pia mater was somewhat œdematous, and in one or two places slightly adherent to the cortex underneath.

The weight of the brain (including the cerebellum and the medulla) was 1,060 grm. The convolutions of the frontal lobes appeared slightly atrophic, but both halves of the brain were symmetrical, and the convolutional pattern was normal. On transverse section the grey matter of the cortex, especially of the frontal lobes, seemed a little thin. By a section across the basal ganglia it was seen that the middle division of the lenticular nucleus on both sides was softened and discoloured over an area about 1 cm. long and broad. The other basal ganglia and the internal capsule were perfectly normal.

There were slight sclerotic patches in the aorta. The liver weighed 1,160 grm., was of firm consistence, and had a knotty, granular surface. Its capsule was slightly thickened in places. On transverse section it was seen to be typically cirrhosed, with numerous nodules of liver-tissue, separated by abundant, small, grey-white bands of connective tissue formation.

The spleen was of normal consistence and its capsule smooth. It was not obviously enlarged.

MICROSCOPICAL EXAMINATION.

Brain.—Nowhere was there any obvious diminution of the medullated fibres, although in a few places in the frontal lobes there might be slight diminution, but it was nothing like so marked as in a case of general paralysis. Where it was present it concerned chiefly the tangential fibres and the supra-radiary network. Over the frontal lobes the pia mater was thickened in places and a little infiltrated with round cells. The neuroglia also appeared a little thickened, especially in the tangential layer, but in any case the changes were not nearly so marked as in general paralysis.

The blood-vessels were distended with blood, and in some places appeared to be widened. The walls of the vessels and of the smallest capillaries were here and there thickened and had a sclerotic or hyaline appearance. In the walls of the vessels were small collections of fine fatty granules, which sometimes bulged into the lumen of the vessel. Very occasionally there were found a few round cells in the adventitial lymph-sheaths. Occasionally also in the blood-vessels, or rather in the perivascular spaces, were yellow-coloured refractile pigment-granules. There were perhaps slight changes in the large pyramidal cells of the cortex; some of them were normal, others seemed small and shrunken or sclerosed, with diminution of their processes and with pigmentary degeneration.

In the vessels which leave the middle cerebral artery to supply the basal ganglia the changes already described were more marked than elsewhere. In one or two places there were very small cellular masses, which looked like thrombi which were commencing to organize.

The pons and the medulla were normal.

Spinal cord.—The spinal cord, examined at various levels, was perfectly normal.

Nerves.—The nerves showed no changes that could be considered of any significance.

Muscles.—The muscles appeared normal, perhaps here and there a little atrophic, but without further degenerative changes.

Liver.—The nodules of cirrhotic tissue contained as a rule from three to five lobules, but sometimes more, and occasionally only one. In the strands of cirrhotic tissue were numerous bile-ducts. Occasionally also there were very fine strands of connective tissue between the columns of liver-cells and sometimes also between individual cells. In these lobules the liver-cells were often quite normal, but others showed fatty degeneration. The whole liver picture bore a marked resemblance to that of "cirrhosis hypertrophica adiposa."

Case 5.—Wilhelm K. was born on August 8, 1870. Up to the age of 3 he suffered from slight attacks, the nature of which is not very definite; apparently they were like *petit mal.* He developed perfectly normally, and at the age of 12 was "fat and well." In the autumn of 1882, for no apparent reason, he began to suffer from slight attacks of giddiness. At the same time he

complained of headache, of pains in his limbs, and of a general feeling of tiredness. About the same time his understanding and his memory seemed to fail. Almost from the outset it was noticed that his gait was somewhat uncertain.

After these symptoms had continued for about a year it was noticed that the patient's speech was becoming defective, and at about the same time his arms became stiff, so that he could not use them properly. Tremor made its appearance in the upper extremities, while the legs also began to get stiff. As a result the latter soon became flexed at the knees and hips.

All these symptoms steadily increased, so that after three or four years the patient became bedridden and had to be fed by others. His speech was limited to a very great extent; it was only rarely that he spoke at all, and then with great difficulty. Saliva constantly escaped from his half-open mouth. Occasionally he had attacks of vomiting.

On December 11, 1888, he was taken to the hospital to be under the care of Professor Homén. It was then remarked that his general look and appearance suggested complete dementia. He did not appear to understand what was said to him, or to pay much attention to what was going on around him. He never spoke at all, but occasionally unintelligible sounds escaped from him; and yet, if he were disturbed or aroused, he could articulate a few words well enough, and even make use of short phrases, of course with difficulty.

The pupils were of medium size and reacted alike slowly to light. Contractures were very pronounced, so much so that the knees were flexed over the abdomen. The arms, too, were flexed. It was possible, however, to straighten the limbs by passive movement, though not to their full extent. As a result of the contractures and of the patient's mental condition he was reduced to utter helplessness. Tremor was almost constantly observable in the hands and arms, occasionally also in the head and in the legs. The musculature was slightly atrophic, and the patient generally much emaciated. The cutaneous reflexes were "weak." The tendon reflexes could not be tested because of the contractures. The patient's condition steadily deteriorated and he died on October 17, 1889, being then 19 years old.

The *post-mortem* examination was held the next day. The contractures of the limbs, more especially of the legs, were extreme. There were bed-sores on the trochanters and elsewhere.

The cranium was thickened; the dura mater also was somewhat thickened. The pia mater was œdematous and in one or two places adherent to the underlying cortex. The weight of the brain was 1,160 grm.; this included the cerebellum. The cerebellum, pons, and medulla weighed together 130 grm. The convolutions of the brain appeared normal, with the possible exception of very slight atrophy of the frontal and central gyri. On transverse section the cortex was possibly somewhat thin in the frontal and central regions. On horizontal section through the basal ganglia, the optic thalamus, internal capsule, and the caudate nucleus were perfectly normal. On the other hand, in the middle of each lenticular nucleus, and symmetrical on the two sides, was a cavity which began about half a centimetre from the upper surface of the nucleus

and was 3 cm. long. More than half of the lenticular nucleus was completely destroyed in breadth, and the cavity which was left contained some serous fluid. The cavity extended to the posterior and inferior end of the nucleus. Round the cavity the tissues were softened for an extent of several millimetres, otherwise the brain seemed perfectly normal.

There were a few sclerotic patches in the aorta.

The spleen was 17 cm. long by 11 cm. broad, and of firm consistence.

The liver was 21½ cm. long, 13 cm. broad, 7½ cm. high. Its surface was markedly cirrhosed. The capsule was in one or two places thickened. On section, the liver was seen to be composed of nodules about the size of lentils or larger, surrounded by strands of connective tissue.

MICROSCOPICAL EXAMINATION.

The fine fibres of the cortex, especially in the tangential and supraradiary layers, were slightly diminished, and the neuroglia was slightly thickened. In the blood-vessels there were here and there small localized endarteritic changes, consisting of minute, granular, more or less homogeneous masses, which often bulged into the lumen of the vessel. These masses lay between the intima and the fenestrated membrane, and occasionally seemed to break through the latter. The changes were most commonly seen in the perforating arteries coming off the middle cerebral artery.

The tissue round the cavity in the lenticular nucleus was softened and crumbling, and infiltrated with cells, but under the microscope no further changes could be seen in the basal ganglia or internal capsule.

The pons, medulla and spinal cord were entirely normal.

Sections of the liver, as in the first case, showed a mixed type of cirrhosis, which was partly multilobular, partly interlobular, partly intralobular. There was marked fatty degeneration of much of the liver-tissue; in the cirrhotic tissue bile-ducts were abundant.

Case 6.—Anna K., the eldest member of the family, was born on July 6, 1862. Her mental and physical development was perfectly good. In her 20th year, towards the end of 1882, exactly the same symptoms as in the case of her brothers made their appearance. She complained of giddiness, headache, general tiredness, and loss of appetite, and at the same time her memory became less good. After about six months or more it was noticed that her walking was a little irregular; at the same time she complained of occasional pains in her legs.

At the age of 22 the muscles began to get stiff and not long after contractures set in at knees, hips and elbows. Articulation became more and more difficult. At this time or a little later tremor appeared, most marked in the arms and hands. All these symptoms steadily increased, so that the patient became helpless and bedridden. She had considerable difficulty in swallowing, and the saliva escaped from her open mouth.

The patient entered the hospital on August 29, 1888. She was completely

helpless, looked demented, lay apathetic in bed, did not speak at all, and paid no attention to what was going on around her. Occasionally she gave vent to a few inarticulate sounds, and yet sometimes she could articulate a few words distinctly, though with difficulty. She died from inflammation of the lungs on October 19, 1888, at the age of 26.

The *post-mortem* examination was held the next day.

The cranium was thickened, as was the dura mater. The pia mater was slightly adherent in one or two places to the cortex underneath.

The frontal convolutions appeared a little shrunken. On section, both lenticular nuclei were softened in their central part and coloured a patchy grey-yellow. The brain with the cerebellum and medulla weighed 1,130 grm.

There were a few sclerotic patches in the aorta.

The spleen measured 12×7 cm. The liver measured 25×14×8 cm.; it was obviously cirrhosed, and on section the nodules of liver-tissue were seen to be about the size of hazel-nuts, though they varied considerably. They were surrounded by firm, grey, fibrous bands.

Microscopical examination of the basal ganglia showed that in the degenerated area of the lenticular nucleus on each side there was commencing disintegration, with degeneration of nerve-cells and fibres.

In the blood-vessels there were a few circumscribed endarteritic changes. Here and there in the degenerated area, slight small-cell infiltration was noticed.

BIBLIOGRAPHY.

A.—Progressive Lenticular Degeneration.

[1] Anton. "Dementia choreo-asthenica mit juveniler knotiger Hyperplasie der Leber," *Münch. med. Wochenschr.*, Nov. 17, 1908, Bd. lv, S. 2369.

[2] Frerichs. "Treatise on Diseases of the Liver," trans. by Murchison, New Sydenham Society, 1860, vol. ii, p. 60.

[3] Gowers. "Diseases of the Nervous System," 1888, vol. ii, p. 656.

[4] *Idem.* "On Tetanoid Chorea and its Association with Cirrhosis of the Liver," *Rev. of Neurol. and Psychiat.*, 1906, vol. iv, p. 249.

[5] Homén. "Eine eigenthümliche Familienkrankheit, unter der Form einer progressiven Dementia, mit besonderem anatomischen Gefund," *Neurol. Centralbl.*, 1890, Bd. ix, S. 514.

[6] *Idem.* "Eine eigenthümliche bei drei Geschwistern auftretende typische Krankheit unter der Form einer progressiven Dementia, in Verbindung mit ausgedehnten Gefässveränderungen (wohl Lues hereditaria tarda)," *Arch. f. Psychiat.*, 1892, Bd. xxiv, S. 191.

[7] Ormerod. "Cirrhosis of the Liver in a Boy, with Obscure and Fatal Nervous Symptoms," *St. Bart. Hosp. Reports*, 1890, vol. xxvi, p. 57.

B.—Involuntary Movements—Tremor, Chorea, Athetosis.

[8] Anton. *See* No. 43.

[9] Berger. *See* No. 45.

[10] Bonhoeffer. "Zur Auffassung der posthemiplegischen Bewegungsstörungen," *Monatsschr. f. Psychiat. u. Neurol.*, 1901, Bd. x, S. 383.

[11] Bristowe. "Clinical Remarks on Tumours involving the Parts in the Neighbourhood of the Third and Fourth Ventricles and the Aqueduct of Sylvius," *Brain*, 1884, vol. vi, p. 167.

[12] DÉMANGE. *See* No. 49.
[13] FREY. "Beiträge zur Lehre der posthemiplegischen Bewegungsstörungen," *Neurol. Centralbl.*, 1905, Bd. xxiv, S. 1104.
[14] GOWERS. "On Athetosis and Post-hemiplegic Disorders of Movement," *Trans. Med.-Chir. Soc.*, 1876, vol. lix, p. 271.
[15] HAENEL. "Zur pathologische Anatomie der Hemiathetose," *Deutsche Zeitschr. f. Nervenheilk.*, 1901, Bd. xxi, S. 28.
[16] HALBAN und INFELD. "Zur Pathologie der Hirnschenkelhaube mit besonderer Berücksichtigung der posthemiplegischen Bewegungserscheinungen," *Arbeit. a. d. Neurol. Inst.*, Wien, 1902, Bd. ix, S. 328.
[17] HERZ. "Zur Frage der Athetose bei Thalamuserkrankungen," *Arbeit. a. d. Neurol. Inst.*, Wien, 1910, Bd. xviii, H. 3, S. 346.
[18] HOLMES. "On Certain Tremors in Organic Cerebral Lesions," *Brain*, 1904, vol. xxvii, p. 327.
[19] HUGHLINGS JACKSON. "The Evolution and Dissolution of the Nervous System," *Brit. Med. Journ.*, 1884, vol. i, p. 591.
[20] KARPLUS und ECONOMO. "Zur Physiologie und Anatomie des Mittelhirns," *Arch. f. Psychiat.*, 1910, Bd. xlvi, S. 275.
[21] KOLISCH. "Zur Lehre von den posthemiplegischen Bewegungserscheinungen," *Deutsche Zeitschr. f. Nervenheilk.*, 1893, Bd. iv, S. 14.
[22] LANDOUZY. *See* No. 57.
[23] LEYDEN. "Fall von Paralysis agitans des rechten Armes in Folge der Entwickelung eines Sarkoms im linken Thalamus," *Virchow's Archiv*, 1864, Bd. xxix, S. 202.
[24] MARBURG. "Die topische Diagnostik der Mittelhirnkrankheiten," *Wien. klin. Wochenschr.*, 25 Mai, 1905, S. 583.
[25] MURATOW. "Zur Pathogenese der Hemichorea postapoplectica," *Monatsschr. f. Psychiat. u. Neurol.*, 1899, Bd. v, S. 180.
[26] *Idem.* "Beitrag zur Pathologie der Zwangsbewegungen bei zerebralen Herderkrankungen," *Monatsschr. f. Psychiat. u. Neurol.*, 1908, Bd. xxiii, S. 510.
[27] VAN OORDT. "Beitrag zur Symptomatologie der Geschwülste des Mittelhirns und der Brückenhaube," *Deutsche Zeitschr. f. Nervenheilk.*, 1900, Bd. xviii, S. 126.
[28] OPPENHEIM und VOGT. *See* No. 40.
[29] PINELES. "Zur Lehre von den Funktionen des Kleinhirns," *Arbeit. a. d. Neurol. Inst.*, Wien, 1899, Bd. vi, H. 6, S. 182.
[30] RHEIN and POTTS. *See* No. 62.
[31] SANDER. "Ein pathologisch-anatomischer Beitrag zur Funktion des Kleinhirns," *Deutsche Zeitschr. f. Nervenheilk.*, 1898, Bd. xii, S. 363.
[32] SCHILDER. "Ueber Chorea und Athetose," *Zeitschr. f. d. ges. Neurol. u. Psychiat.*, 1911, Bd. vii, H. 3, S. 219.
[33] SHARKEY. "Spasm in Chronic Nerve Disease," Goulstonian Lectures, *Brit. Med. Journ.*, 1886, vol. i, p. 531.

C.—SYNDROME OF THE LENTICULAR NUCLEUS AND CORPUS STRIATUM.

[34] DANA. "The Functions of the Corpora Striata, with a Suggestion as to a Clinical Method of studying them," *Journ. Nerv. and Ment. Dis.*, Feb., 1908, p. 65.
[35] FRANCESCHI. "Sul meccanismo patogenetico del riso e del pianto spastico e sulla funzione motoria del nucleo lenticolare," *Riv. di patol. nerv. e ment.*, 1905, p. 249.
[36] FREUND und VOGT. "Ein neuer Fall von Etat marbré des Corpus striatum," *Journ. f. Psychol. u. Neurol.*, 1911, Bd. xviii, S. 489.
[37] MILLS and SPILLER. "The Symptomatology of Lesions of the Lenticular Zone, with some Discussion of the Pathology of Aphasia," Univ. of Penn., Contrib. from the Depart. of Neurol., 1907, vol. iii.
[38] MINGAZZINI. "Sulla sintomatologia della lesioni del nucleo lenticolare," *Riv. sper. di freniatr.*, 1901, p. 489, 1902, p. 317.
[39] *Idem.* "Das Linsenkernsyndrom," *Zeitschr. f. d. ges. Neurol. u. Psychiat.*, 1911, Bd. viii, H. 1, S. 85.

[40] OPPENHEIM und VOGT. "Wesen und Localisation der kongenitalen und infantilen Pseudobulbärparalyse," *Journ. f. Psychol. u. Neurol.*, 1911, Bd. xviii, S. 293.

[41] PIAZZA. (Abstract in *Rev. Neurol.*, 1906, p. 934.) "Contribution clinique et anatomo-pathologique aux lésions du noyau lenticulaire," *Riv. d. patol. nerv. e ment.*, Feb., 1906, vol. xi, p. 71.

[42] VOGT (CÉCILE). "Quelques considérations générales à propos du syndrome du corps strié," *Journ. f. Psychol. u. Neurol.*, 1911, Bd. xviii, Ergänzungsheft 4, S. 479.

D.—CORPUS STRIATUM GENERALLY.

[43] ANTON. "Ueber die Beteiligung der grossen basalen Gehirnganglien bei Bewegungsstörungen und insbesondere bei Chorea," *Jahrbücher f. Psychiat.*, 1896, Bd. xiv, H. 1.

[44] BECHTEREW. "Pseudomelia paraesthetica als Symptom einer Cerebralaffection im Gebiete des Linsenkernes," *Neurol. Centralbl.*, 1905, Bd. xxiv, S. 786.

[45] BEBGER. "Zur Kenntniss der Athetose," *Wien. klin. Rundschau*, 1901, S. 751.

[46] BRAMWELL. "Case of Cancer of the Right Lobe of the Cerebellum and Left Lenticular Nucleus; Marked Vertigo; no Paralysis," *Brain*, 1888, vol. x, p. 503.

[47] CANFIELD and PUTNAM. "A Case of Acute Hemiplegic Chorea, with Autopsy and Remarks," *Boston Med. and Surg. Journ.*, Sept. 4, 1884, p. 220.

[48] CZYHLARZ und MARBURG. "Weitere Bemerkungen zur Frage der cerebralen Blasenstörungen," *Wien. klin. Wochenschr.*, 1902, Nr. 31, S. 788.

[49] DÉMANGE. "Contribution à l'étude des tremblements prœ- et post-hémiplégiques," *Rev. de Méd.*, 1883, p. 871.

[50] EISENLOHR. "Ueber acute Bulbär- und Ponsaffectionen," *Arch. f. Psychiat.*, 1879, Bd. ix, S. 1 (Obs. 9).

[51] FERRAZINI et PAOLI. "Un cas d'autopsie de maladie de Thomsen," Ref. in Etienne. *See* No. 68.

[52] FULLER and BROWNING. "Pseudobulbar Paralysis; Bilateral Apoplexy of the Lenticular Nuclei," *Med. Rec.*, Nov. 1, 1884, p. 487.

[53] VAN GEHUCHTEN. "Lésion de la zone lenticulaire gauche, sans troubles de la parole," *Névraxe*, 1910, vol. xi, p. 7.

[54] GRASSET. "D'une variété non décrite de phénomène post-hémiplégique," *Progrès médical*, Nov. 13, 1880, p. 927.

[55] HEBOLD. "Welche Erscheinungen machen Herderkrankungen im Putamen des Linsenkerns?" *Arch. f. Psychiat.*, 1892, Bd. xxiii, S. 447.

[56] HUTCHINSON. "A Case in which Paralysis of the Sphincters and Incontinence of Urine were, together with Torpid Intellect, the Chief Symptoms of Symmetrical Disease of the Corpora Striata," *Brain*, 1888, vol. x, p. 223.

[57] LANDOUZY. "Note sur un cas d'athétose; observation; autopsie," *Progrès médical*, 1878, vol. vi, p. 79.

[58] LÉPINE. "Paralysie glosso-labiée cérébrale; rire et pleurer spasmodiques," *Rev. de Méd.*, 1896, p. 263.

[59] *Idem.* "Note sur la paralysie glosso-labiée cérébrale en forme pseudobulbaire," *Rev. mens. de méd. et de chir.*, 1877, p. 909.

[60] LÖWY. "Symmetrische Erweichungsherde beider Hemisphären im Kopfe des N. caudatus und in ausserem Gliede des Linsenkernes, mit Muskelrigidität," *Deutsche med. Zeitung*, 1903, Bd. xxiv, S. 789.

[61] REICHEL. "Zur Pathologie der Erkrankungen des Streifenhügels und Linsenkern," *Wien. med. Presse*, 1898, S. 752.

[62] RHEIN and POTTS. "Post-apoplectic Tremor: Symmetrical Areas of Softening in both Lenticular Nuclei and External Capsules," *Journ. Nerv. Ment. Dis.*, 1907, p. 757.

[63] ROSS. "Labio-glosso-pharyngeal Paralysis of Cerebral Origin," *Brain*, 1882-3, vol. v, p. 145.

[64] SCHILDER. *See* No. 32.

[65] WEIR MITCHELL. "Post-paralytic Chorea," *Amer. Journ. Med. Sci.*, 1874, vol. lxviii, p. 342.

E.—Spasticity, Hypertonicity, Contracture.

[66] Babinski. "De l'équilibre volitionnel. statique et cinétique," *Rev. Neurol.*, 1902, vol. x, p. 470.

[67] Bechterew. "Hemitonia postapoplectica," *Deutsche Zeitschr. f. Nervenheilk.*, 1899, Bd. xv, S. 437.

[68] Etienne. "Syndrome hémi-tonoclonique post-hémiplégique," *L'Encéphale*, 1907, vol. ii, p. 1.

[69] Handelsmann. "Ueber die neurotonische elektrische Reaktion (Ein Fall von Syringomyelie mit neuro- und myotonischer Reaktion)," *Neurol. Centralbl.*, 1911, Bd. xxx, S. 418.

[70] Kaiser. "Myotonische Erscheinungen bei Athetose," *Neurol. Centralbl.*, 1897, Bd. xvi, S. 674.

[71] Lévi. "Le syndrome myotonique," *Sem. méd.*, 1905, vol. xxv, p. 541.

[72] Lewandowsky. "Bemerkungen über die hemiplegische Contractur," *Deutsche Zeitschr. f. Nervenheilk.*, 1905, Bd. xxix, S. 208.

[73] Luciani. "Il Cerveletto," Florence, 1891.

[74] Mann. "Wesen und Entstehen der hemiplegischen Kontraktur," *Monatsschr. f. Psychiat. u. Neurol.*, 1898, Bd. iv, S. 45.

[75] Pfeiffer. "Ein klinischer Beitrag zur Lehre von der Hemitonia apoplectica," *Neurol. Centralbl.*, 1901, Bd. xx, S. 386.

[76] Thomas. "Le Cervelet," *Thèse de Paris*, 1897.

F.—Pseudobulbar Paralysis, Dysarthria, Dysphagia.

[77] Brissaud. "Le rire et le pleurer spasmodiques," in "Leçons sur les maladies nerveuses," Paris, 1895.

[78] Comte. "Des paralysies pseudobulbaires," *Thèse de Paris*, 1900.

[79] Halipré. "La paralysie pseudobulbaire d'origine cérébrale," *Thèse de Paris*, 1894.

[80] Hartmann. "Die Pathologie der Bewegungsstörungen bei der Pseudobulbärparalyse," *Zeitschr. f. Heilk.*, 1902, Bd. xxiii, S. 256.

[81] Jakob. "Die Pathogenese der Pseudobulbärparalyse," *Arch. f. Psychiat.*, 1909, Bd. xlv, S. 1097.

[82] Lebesche. *Thèse de Paris*, 1890.

[83] Marshall and Jacob. "Pseudobulbar Paralysis due to Bilateral Tuberculous Tumours," *Brit. Journ. Children's Diseases*, 1904, vol. i, p. 199.

[84] Raymond et Lejonne. "Paralysie pseudobulbaire chez un enfant," *Rev. Neurol.*, 1906, vol. xiv, p. 379.

[85] Ross. *See* No. 63.

[86] Weisenburg. "Pseudobulbar Palsy," Univ. of Penn., Contrib. from Lab. of Neuropath., 1905.

G.—Paralysis Agitans.

[87] Jelgersma. "Neue anatomische Befunde bei Paralysis agitans und bei chronischer Chorea," *Neurol. Centralbl.*, 1908, Bd. xxvii, S. 995.

H.—"Kernicterus."

[88] Beneke. "Ueber den Kernikterus des Neugeborenen," *Münch. med. Wochenschr.*, 1907, Bd. liv, S. 2023.

[89] Esch. "Ueber Kernikterus der Neugeborenen," *Zentralbl. f. Gynäk.*, 1908, S. 969.

[90] Pfannenstiel. "Ueber den habituellen Ikterus gravis der Neugeborenen," *Münch. med. Wochenschr.*, 1908, Bd. lv, S. 2169.

[91] Schmorl. "Zur Kenntnis des Ikterus neonatorum, insbesondere der dabei auftretenden Gehirnveränderungen," *Verhandl. d. deutsch. pathol. Gesellschaft.*, Jena, 1904, sechste Tagung, S. 109.

ADDENDUM.

WITHIN a few days of the publication of this monograph my attention has been drawn to a paper, by Völsch, on "Pseudosclerosis" (*Deutsche Zeitschr. f. Nervenheilk.*, September, 1911, Bd. xlii, S. 335), in which that author describes a case diagnosed, not without reserve, as pseudosclerosis, which in many ways resembles progressive lenticular degeneration. The patient was a girl, aged 17, of previous normal development, who for about two years, or rather more, had suffered from rhythmical tremors of the limbs and trunk, occasional paroxysmal attacks of violent tremor, and spastic contractures of the extremities. The mouth was always open; dysarthria and dysphagia were present; the facies was immobile. There was no actual paresis, and sensibility was intact. The plantar reflexes were flexor in type, while the abdominal reflexes were preserved. There was some slight general mental impairment and dulness. The patient died from scarlatina at the age of 17. *Post-mortem*, there was marked atrophic cirrhosis of the liver, which had not been diagnosed during life, and considerable enlargement of the spleen. The brain was hardened and cut in slices, but no abnormality was found. Völsch considers the case to be probably a variety of the pseudosclerosis of Westphal and Strümpell, though he admits it differs in several important particulars.

It will be clear to the reader that a case of this description bears the closest analogies to those here reported, and this being so, it is peculiarly unfortunate that the pathological details are so meagre. There is no account of the direction of the slices into which the brain was cut, an important matter when it is remembered that an atrophic but not disintegrated putamen might not thus be remarked; there is no note of any microscopical investigation of the corpus striatum; the cortex and cord apparently were all that were examined microscopically, and they were found to be normal. Notwithstanding the dearth of information, this case, I believe, comes under the category of those which I have described.

Pseudosclerosis is a nosological conception which has been utilized to include very varying cases, in not a few of which pathological examination has been so restricted as to be valueless. But among

those thus classified there has been at least one other, besides Völsch's case, in which cirrhosis of the liver occurred, complicated, it is true, with diabetes (Fleischer, *Münch. med. Wochenschr.*, 1909, S. 1120). In view of the material collected in the present article, it is desirable that the unsatisfactory and makeshift expression "pseudosclerosis," which was coined for certain cases which were said to resemble disseminated sclerosis clinically, but not pathologically, should be abandoned, and that reinvestigation of the subject should be undertaken.