DYSSYNERGIA CEREBELLARIS MYOCLONICA—PRIMARY ATROPHY OF THE DENTATE SYSTEM: A CONTRIBUTION TO THE PATHOLOGY AND SYMPTOMATOLOGY OF THE CEREBELLUM.[1]

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CHAPTER I.—INTRODUCTION.

SOME years ago, under the title "Dyssynergia Cerebellaris Progressiva, or Chronic Progressive Cerebellar Tremor" [10] I directed attention to a peculiar disorder of motility, which I regarded as a definite clinical type of nervous disease.

This affection was characterized by generalized intention tremors, which began as a local manifestation and gradually extended to other parts of the voluntary muscular system. The extremities, and more especially the arms, showed the greatest degree of involvement.

The coarse ataxic-tremor disturbance which characterized the dis-

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order was only present when the muscles were in action, and ceased entirely during relaxation and rest. It was, therefore, volitional in character and of the "intention tremor type." Another peculiar feature was the severe involvement of the finer co-ordinated movements of the extremities, while the coarser and more massive movements underlying station and locomotion were but little affected.

When this tremor disturbance was subjected to careful analysis there was found associated with it a disorder of muscle tone and of the ability to measure direct and associate muscular movements, the clinical manifestations of which were dyssynergia, dysmetria, adiadokokinesis, hypotonia and asthenia. All of these symptoms, including the volitional tremor, which was an extreme expression of the underlying disturbance of muscle tone and synergy, showed the existence of a fundamental disorder of cerebellar function.

I, therefore, regarded the affection with its progressive tendency, chronic course and well-defined cerebellar symptomatology as "an organic disease caused by degeneration of certain special structures of the cerebellar mechanism, which were concerned in the regulation of the tonus and synergies of muscles."

Since my original publication, I have had occasion to observe another group of cases which combined the symptomatology of dyssynergia cerebellaris progressiva and myoclonus-epilepsy. There was the progressive dyssynergia characteristic of a cerebellar disorder, in association with epilepsy and myoclonus. Here, as in the group of cases uncomplicated by myoclonus-epilepsy, the movements of the extremities showed the greatest degree of disturbance.

This form of dyssynergia, which I would term dyssynergia cerebellaris myoclonica, I have also observed in association with Friedreich's ataxia, a combined cerebello-spinal involvement, which is not infrequent in the history of cerebellar system disease. In one of these cases careful pathological investigations were made which throw considerable light on the origin and anatomical basis of the cerebellar portion of the symptomatology. On the basis of these studies I would refer the progressive dyssynergia to a primary atrophy of the efferent dentate system of the cerebellum, and would regard this system as the essential neural mechanism underlying the production of the cerebellar or intention tremor.

In conclusion, I will state my views on the relation of the cerebellum to the static or posture system of motility, and the bearing which this conception has on the interpretation of cerebellar function.

CHAPTER II.—DYSSYNERGIA CEREBELLARIS PROGRESSIVA MYOCLONICA: A FORM OF PROGRESSIVE CEREBELLAR TREMOR ASSOCIATED WITH MYOCLONUS-EPILEPSY.

Critical Report of Four Cases.

CASE 1.

Summary.—Myoclonus-epilepsy began at the age of 17, and was followed five years later by symptoms of dyssynergia cerebellaris progressiva, viz., generalized intention tremors and scanning speech, associated with dysmetria, dysdiadokokinesis, hypotonia and asthenia.

The patient, a man aged 30, single and a telegraphist by occupation, was referred to the Neurological Institute, in May, 1918, and was admitted to the service of Dr. Pearce Bailey. I am indebted to Dr. Bailey for the privilege of observing and reporting the case.

Family history.—His father was a periodical drinker and two of the father's uncles were alcoholic. An aunt on the father's side was subject to fainting attacks of rather doubtful nature and which were not called epileptic by the family. Their character could not be determined with certainty. His mother is living and in good health. Parents were not related. One sister is alive and well. A brother died in early life. No other member of the family, so far as he knows, has had any disease similar to the one from which he is suffering.

The previous history shows nothing unusual. Childhood was normal, he did good work at school and was quite up to the average in his mental development. He had measles and whooping-cough in early life. There was no history of trauma, venereal disease or of alcoholic excesses.

Onset.—The first symptoms of his disease appeared at the age of 17. At this time he had an epileptic seizure which was characterized by clonic muscular spasms of the right arm and leg, which developed while wrestling and lasted only a few minutes. He had two such attacks, neither of which were associated with complete unconsciousness but in both he became dizzy and fell to the ground. After these initial seizures the subsequent attacks were always accompanied by complete loss of consciousness. They were nearly always preceded by a motor aura, consisting of a progressive spasm of the right arm and leg, which terminated in unconsciousness, and was followed by a general convulsion. The tongue was often bitten, and there were occasional incontinence of urine and the other manifestations of a major epileptic seizure. These grand-mal attacks were comparatively infrequent, occurring only three or four times a year, and at one time there was a free interval of nearly three years.

When he was 19 years of age, that is, two years after the first epileptic seizure, the myoclonic jerks made their appearance. These were usually worse in the early morning hours and gradually increased in extent and intensity. He states that they were usually diminished by the use of alcohol, and the

patient sometimes took this means of relieving their severity. The myoclonus first appeared in the hands and arms and gradually extended to the trunk and lower extremities. Subsequently, the myoclonus became so severe that he was occasionally thrown to the ground and on one of these occasions he broke his nose.

Five years after the onset of the myoclonus-epilepsy the intention tremor made its appearance in the arms. This gradually increased in severity and later the speech became affected, and the legs showed evidences of involvement.

There has been no headache, no diplopia and he states no special impairment of memory. Preceding the epileptic attacks there is a whirring sensation in the head but otherwise no vertiginous seizures. The myoclonus is increased by mental stress and worry, and varies in its intensity from day to day. He has good days when the involuntary jerks and starts are in abeyance and other days when they are very severe.

Physical examination.—Shows a well-developed muscular man. The speech is slow and scanning in character and of the cerebellar dysarthric and explosive type. There is a well-marked, typical intention tremor of both upper extremities, similar in all respects to that observed in multiple sclerosis. In addition there is also a typical intention tremor of both lower extremities. Associated with the intention tremor are evidences of dysmetria and dysdiadokokinesis.

There is no loss of the gross motor power of arms or legs and no muscular atrophy. There is, however, in the arms, some diminution of the power to maintain fixed muscular contractions and postures except for short periods of time, due to tremor and asthenia. For example, when he extends the arm from the body in abduction, and attempts to hold it in this position, there ensues a coarse ataxic tremor and after a brief effort the arm is dropped to the side, in this respect simulating the behaviour of the intention tremor in multiple sclerosis. There is difficulty in maintaining a fixed posture of the upper extremities except for short periods of time. There is also a moderate degree of hypotonia in both upper and lower extremities. The Stewart-Holmes sign of cerebellar hypotonia is however not demonstrable.

The tendon reflexes of both upper and lower extremities are present, active and equal on the two sides. There is no ankle clonus, no patellar clonus and the plantar reflex is of the normal flexor type (no Babinski response). The cremasteric and abdominal reflexes are present and equal on the two sides. There is no history of pain or of paræsthesias. All sensations both superficial and deep are normal.

The pupils are equal and react to light and accommodation. The ocular excursions are normal and there is no nystagmus. Fundi negative. The innervation of the face, tongue, soft palate and muscles of mastication are also normal. Save for occasional myoclonic jerks there is no Rombergism and the station is normal. The spine is normal in contour and in movement.

During the course of the examination there are frequent myoclonic starts or jerks in both upper and lower extremities and trunk. This tendency is

increased or may be induced by voluntary movement, and this together with the intention tremor produces a very grave disorder of muscular co-ordination.

When lying on the back patient is relaxed and perfectly quiet, but any attempt at movement is likely to initiate myoclonic twitchings of the face, extremities or trunk. This tendency is increased by talking, or indeed by any form of volitional movement. In the recumbent position he can elevate both the upper and lower extremities, and hold them in this position with closed eyes without developing ataxic movements. The myoclonic jerks also occur spontaneously apparently without the intervention of volitional effort.

He is able to stand and walk, but does so with great caution and some uncertainty as if anticipating a myoclonic jerk. The intention tremors of the arms and legs occur with all volitional movements and present all the typical characteristics of this form of tremor. It is readily distinguished from myoclonic jerks although frequently accompanied by them. Associated with the intention tremor are typical dysmetria and dysdiadokokinesis. The gait and station, while showing some uncertainty, are not markedly titubating in character and the evidences of cerebellar disorder affect deeply the higher forms of motility, viz., speech and the volitional movements of the extremities (appendicular dyssynergia).

The heart and lungs are normal. Abdominal palpation is negative. There is no demonstrable enlargement of the hepatic area, and no evidences of abnormal pigmentation of the skin or cornea. Urine normal; Wassermann test of blood negative.

Comment.—This patient presents in addition to the symptoms of myoclonus-epilepsy a chronic progressive dyssynergia of cerebellar origin. With the scanning speech and intention tremors of both upper and lower extremities there are the associated manifestations of cerebellar disease, viz., dysmetria dysdiadokokinesis, hypotonia and asthenia. With the exception of epilepsy, myoclonus and dyssynergia there are no other evidences of organic disease of the nervous system. It is of interest to note that the evidences of dyssynergia are appendicular rather than trunkal in distribution and that higher types of movement are chiefly affected. There was no familial history of either myoclonus-epilepsy or cerebellar disease.

Case 2.

Summary.—A girl, aged 19; onset of myoclonus-epilepsy, at the age of 7. Associated with this is a progressive dyssynergia of cerebellar origin, affecting more especially the speech and extremities.

This patient is 19 years of age, and single. She was admitted to the Craig Colony for Epileptics on January 14, 1918, and is still under observation in that institution, where I saw her in consultation with Dr. Doolittle of the Colony Staff.

Family history.—Father has been excessive in the use of alcohol. Her mother is in good health. Parents are not related. She has three brothers

and two sisters, all in good health. There is no family history of any similar nervous disorder.

Personal history.—The patient was born at full term following a labour lasting forty-eight hours. The delivery was said to have been natural. Among possible pre-natal influences may be mentioned her father's alcoholism and mother's worry over family affairs. There was no paralysis or spasm immediately after birth. Her mind developed naturally during infancy and childhood, and she was considered very bright in school. She had whooping-cough at 10 years, measles at 13 years, and diphtheria at 14.

Present illness.—At the age of 7 it was first noticed that her hands would shake and jerk while feeding herself or trying to pick up things. This tendency to myoclonus continued and gradually increased in extent and severity, finally involving, in addition to the arms, the legs, trunk, and even the facial musculature.

Three years later, when she was 10 years old, she had her first epileptic seizure. These attacks recurred every three or four months. They were diurnal and of the grand-mal type. At the present time she averages about six grand-mal seizures a year. They are of typical character, and are frequently associated with biting of the tongue and incontinence of urine. It was difficult to obtain any very definite statement as to the time of the appearance of the intention tremor, because of the existence and severe nature of the myoclonic phenomena which tended to mask the other motor disorder.

For the last five years, however, a coarse ataxic tremor of the arms and legs has been present on volitional movements and the speech has been jerky, irregular, explosive. These symptoms have grown gradually worse. It is more than probable that the characteristic symptoms of a cerebellar disorder were present before the fourteenth year, and were overshadowed by the myoclonia.

Physical examination (February, 1918).—During the course of the examination, while patient is seated in a chair, there are frequent sudden myoclonic jerks or starts, which may appear spontaneously, but usually precede or follow some volitional effort. These may appear in the arms, trunk, legs, or face; as a rule, there is a single coarse jerk or start, and then an interval—occasionally a small series of myoclonic starts occur in rapid succession. These movements are brusque, sudden, and involve synergic groups of muscles and produce a considerable locomotor effect. On arising from a sitting posture there is at first a slight unsteadiness and an effort to restore the equilibrium by standing upon a broad base with balancing. While walking, the harmony of movement is frequently broken by coarse myoclonus jerks which throw her to one side, causing a loss of balance.

These coarse myoclonus jerks appear in the trunk and arms and legs. They also occur while sitting quietly in a chair, producing sudden brusque jerks of the trunk or extremities. A slight flicker of myoclonic character is occasionally observed in the face. The myoclonus is very apt to occur just before, apparently initiated by the response to a voluntary movement, such as lifting up the arm, placing finger on the tip of the nose, or a movement of a

leg. At certain times, and on certain days, they are much more severe than at others, and in the morning they occasionally cause her to toss about in the bed so that she almost falls out. This patient's myoclonic movements sometimes continue during sleep and disturb her rest to a considerable extent. The abdominal muscles are also occasionally the seat of spasm. The myoclonic movements of the extremities are often symmetrical, both sides being simultaneously involved. The difficulties of gait and station are very much increased by the tendency to myoclonus, as all of the usual muscular activities of standing and walking in themselves produce myoclonus, and are the cause of constant uncertainty and inco-ordination.

She is able to stand alone, and there is no Rombergism. She walks on a rather broad base, lifting the foot too high with jerky, irregular ataxic-like movements of the legs (dysmetria). The attitude of the trunk is also somewhat oscillating, showing a slight tendency to balancing. The spine is straight, and there is no scoliosis.

A cerebellar or intention tremor is present in both upper extremities, more particularly on the left side. It is of the same character as the intention tremor of multiple sclerosis and is brought out conspicuously by the finger-nose test. On the performance of this test there is the coarse atactiform shaking which increases in intensity as the finger approaches the tip of the nose. And there is the quick jerking away movement of the fingers from the tip of the nose, as in true intention tremor. Well marked adiadokokinesis and evidences of dysmetria are also present on both sides.

In the recumbent posture there is also dysmetria in the heel-knee test, and volitional movements are irregular, jerky and of the cerebellar ataxic type. The movements during these tests are frequently interrupted by myoclonic jerks. There is no noteworthy hypotonia of the extremities and the Stewart-Holmes sign of hypotonia is absent.

The tendon reflexes of the arms (supinator, biceps and triceps jerks) are present and not exaggerated. The knee-jerks are active and equal on the two sides. Both Achilles jerks are present and equal. There is no clonus. The abdominal reflexes are present and equal. The plantar reflexes are also present and of the normal flexor type (no Babinski).

The pupillary reflexes are normal. The ocular excursions are normal and there is no nystagmus. Fundi normal. The innervation of the face, tongue, soft palate and muscles of mastication are normal.

The speech shows well-marked dysarthria of the cerebellar type. It is jerky, explosive and at times scanning.

There is no Romberg symptom and no ataxia of station develops on closure of the eyes. In the recumbent posture both the upper and lower extremities may be elevated and held in this position with closed eyes without the development of ataxic movements.

Sensation.—The superficial sensibility is normal. The sense of touch, pain and temperature are well preserved. The deep sensibility is also normal and there is no disorder of the sense of posture.

There is no disturbance of the sphincter control of the bladder or rectum.

The intelligence shows some general reduction and retardation. There is loss of memory and slowness of thought and action. Judgment is poor. In the Binet-Simon test she is rated at 9 years.

The heart and lungs are normal. The urine is normal. Wassermann test of the blood is negative. There are no evidences of abnormal pigmentary deposits on the skin or at the sclero-corneal junction.

Comment.—With the exception of myoclonus-epilepsy and progressive dyssynergia there are no other evidences of organic disease of the nervous system. The chief disorder of cerebellar function is that affecting articulation and the movements of the extremities. The gait and general equilibrium also show some disorder of cerebellar function, which is accentuated by the severe type of myoclonia which is present.

In this case the dyssynergia while preponderantly appendicular in distribution also involves to some extent the trunkal musculature. As in the previous case, there was no history of the familial occurrence of either myoclonus-epilepsy or cerebellar disease.

CASE 3.

Summary.—Myoclonus-epilepsy of twenty-six years' duration. Associated with symptoms of dyssynergia cerebellaris progressiva, viz., cerebellar dysarthria, intention tremor, dysmetria and adiadokokinesis, affecting chiefly the volitional movements of the extremities.

This patient was a man, aged 38, single, an inmate of Craig Colony for Epileptics, where I saw him in consultation with Dr. Shaw of the Colony staff.

Family history.—Parents are living and in good health, patient is an only child of his fraternity. He has one half sister (mother's daughter by first marriage), aged 42, who is married and in good health. Careful inquiry by letters and interviews failed to reveal any history of epilepsy or other nervous disorder among the relatives.

Personal history.—The history of the birth, of infancy and of childhood were negative up to the age of 12 years. He had whooping-cough at 8, and measles at 9. There were no untoward symptoms during these infections, which would indicate involvement of the central nervous system. School progress was about the average, and at the age of 16 he left school to work on a farm. He continued this occupation up to the time of his admission to the Colony in the summer of 1912. His habits were moderate, he used tobacco in moderation and beer occasionally. There was no history of injury or of venereal infection.

History of the disease.—Epilepsy: his first seizure occurred at the age of 12 years. He was on his way from school, stopped to tie his shoe-string, and fell over in a convulsion. "Rush of blood to the head" was the assigned cause. Soon after this, myoclonic jerks and twitchings made their appearance. These gradually increased in severity and frequency and were especially

severe in the mornings. Myoclonia was usually greatly exaggerated before convulsive phenomena.

His general nervousness and the severe myoclonia were the reasons for his seeking admission to the Craig Colony in 1912.

Upon admission he was in good general health, and weighed 187 lb. He was "nervous and unstable." There were myoclonic jerks involving the head, trunk, upper and lower extremities.

His general intelligence was fair.

During the six years of his Colony residence, he has slightly deteriorated mentally, and has lost weight, but not rapidly. The myoclonia has greatly increased. The speech defect which was slight on admission has become intensified. There are exhaustion states following severe attacks of myoclonia, which at times may exist for days, and are quite general in their distribution.

It is definitely established that during the early years of his disorder he had severe grand-mal seizures, the tongue was bitten and there are scars about the face and scalp due to injuries received by falling during attacks. From 1912 to 1916 there are recorded occasional seizures, which appear on the regular Colony records, but most careful investigation fails to reveal, even from those in daily contact with him, that he has had attacks other than myoclonia in recent years. The present nurse in charge of his cottage, who has observed him for the greater part of five years, denies the occurrence of seizures, and states that the only manifestations of his illness are the "jerks and tremors." It is quite certain that the years of 1916, 1917 and 1918 have found him free from epileptic seizures, as he has been under close observation during that time. He has averaged during this period about two weeks per year in bed as a result of myoclonia, which made it impossible for him to get about, or even to feed himself.

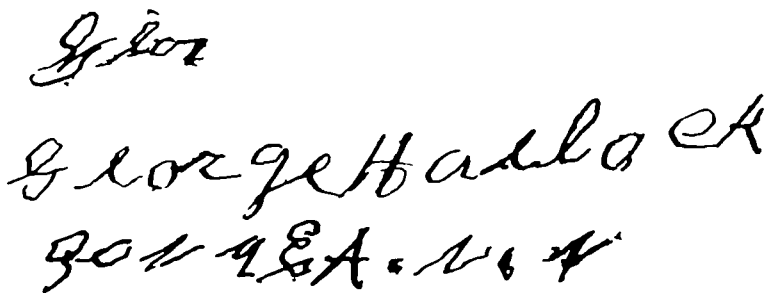
Physical examination. — Patient is a muscular, well-developed man. Station is steady and there is no Romberg symptom on closing the eyes. The spine is normal in contour and movements. The gait shows a slight clumsiness and awkwardness, especially on turning corners or facing about suddenly. At these times there is a slight tendency to uncertainty and the smooth harmony of balance and locomotion is somewhat disturbed. There is, however, no definite or distinct tendency to titubation and the slight disorder of gait and station might be regarded as merely clumsiness were it not for the existence of other and more characteristic cerebellar symptoms in the more delicate movements of the extremities.

The pupils are equal and react to light and accommodation. The ocular excursions are normal and there is no nystagmus (no history of diplopia). The other cranial nerves are negative. Fundi are normal.

Speech is of the cerebellar type, slow, of scanning character, and at times explosive. The tongue is protruded in the median line, without tremor. The innervation of the face, masseters and soft palate are normal. Frequently during the examination coarse myoclonic jerks and jumps occur in the extremities and trunk. These may be spontaneous but are particularly likely to

be initiated by any volitional effort or movement. At times the myoclonus occurs immediately after the cessation of a movement. Occasionally it is symmetrical on the two sides of the body, but both in the arms and legs independent myoclonic contractions are common. As in other cases the face is also occasionally involved.

There is no diminution of the gross motor power of the extremities and no evidences of muscular atrophy. On attempting to place the index finger on the tip of the nose a well-marked intention tremor is developed, which is more pronounced on the left side. This varies somewhat in intensity. At times there is present the coarse, slow, ataxic movement of dyssynergia which increases as the finger approaches the nose, on other occasions it has more the character of the typical intention tremor of multiple sclerosis. Evidences of dysmetria and typical adiadokokinesis are also present in both upper extremities, more particularly on the left side.



Patient's signature July 23, 1918, during "quiescent period" of the myoclonia.

In the lower extremities, evidences of cerebellar ataxia (dyssynergia and dysmetria) are also elicited when volitional movements are attempted, such as placing the heel upon the knee. There is no definite hypotonicity of the muscles of either arms or legs, and the Stewart-Holmes sign of hypotonia is absent.

Reflexes.—The arm jerks (supinator, biceps and triceps jerks) are present and active. The knee jerks and Achilles jerks are also present and active. There is no clonus. The skin reflexes are normal. The abdominal and cremasteric reflexes are elicited and the plantar reflexes are present and of the flexor type (no Babinski).

All sensations, both superficial and deep, are normal. The sense of position is quite normal in both upper and lower extremities. Abdominal palpation is negative and there is no enlargement of the hepatic areas, no abnormal pigmentary deposit of skin and sclera. The heart and lungs are normal. Urine is normal. Wassermann test of the blood is normal.

Comment.—In this patient, as in the others, there was difficulty in determining the approximate age of onset of the dyssynergia. The myoclonus-epilepsy is itself such a formidable condition and causes so severe a disturbance

of motility that it rather tends to mask the other disorder. With the exception of myoclonus-epilepsy and dyssynergia no other symptoms of organic disease of the central nervous system could be found. Symptoms indicative of multiple sclerosis, Friedreich's ataxia or gross cerebellar disease were not present. I would therefore regard the condition as one of dyssynergia cerebellaris associated with myoclonus-epilepsy.

There was no familial history of either disorder.

CASE 4.

Summary.—A girl 15 years of age with nocturnal epilepsy, myoclonia and slight cerebellar dyssynergia of three years duration.

A young girl, 15 years of age, a private patient, first came under my care in July, 1921. The family history, so far as could be elicited, was negative. The father, a professional man, died as the result of an accident. Up to the time of his death, at the age of 45, he was in good health and had never presented any symptoms of nervous or mental disease. Mother is living and well. There is no history of epilepsy, myoclonia or other organic nervous disease in their forebears. The parents were not related.

Previous history.—Patient is an only child, born at term, normal pregnancy and non-instrumental delivery. She was breast fed for a year and with the exception of digestive disturbances in early life was a normal infant. No infantile convulsions. Menses began at the age of 12, and are quite irregular. She was sent to school at the usual age and is of average intelligence.

History of present illness dates back about three years and began with what have been called nightmares. She awakens in the night with a scream and passes into general convulsive attack with unconsciousness, frothing at the mouth, lasting several minutes, and followed by a period of mental confusion. At first these attacks were infrequent but later they increased in number and severity and now average once a week, sometimes oftener. Two years ago, that is, one year after the beginning of the nocturnal epileptic seizures, curious muscular jerks or twitchings made their appearance. At first these were not severe and were more marked on certain days, usually the day before the nocturnal seizures. The arms, legs and trunks were variously affected, later speech became involved and there was a slight tendency to myoclonic waves and twitching of the face. This tendency to myoclonus has gradually grown worse and on bad days it is rather difficult for her to walk alone and use her arms in dressing and eating—on these occasions she usually remains in bed.

On these bad days she sometimes falls to the ground while walking or standing, the legs suddenly giving way under her. On two occasions she had severe falls of this character, apparently associated with momentary blurring of consciousness. The patient insists, however, that in these falls there is no vertiginous sensation or momentary lapse of consciousness and she simply suddenly loses the ability to stand upright, her legs giving way under her. On one occasion when I was testing her gait and equilibrium she plunged quite

suddenly to the floor, all of a heap, striking her chin rather heavily. She immediately rose to her feet and was a little shaken from the sudden and severe fall, but as far as I could determine there was no obscuration of consciousness or pallor, as one observes in petit mal. The attack was caused by a sudden release of the muscular mechanism which underlies the posture of standing and is probably a massive expression of the myoclonia. In one of these she suffered quite a severe laceration of the scalp. As a rule the myoclonia is most severe a few hours before an attack and it is usually possible to foretell the epileptic seizures by this aggravation of the myoclonic phenomena.

A nurse who has slept in the room with the patient for a number of months gives the following description of the seizure. "An attack, or nightmare, is usually preceded by an unsteady afternoon and evening: a difficulty in eating and talking and an inability to walk unaided is shown at these times. The nightmare usually begins with a series of screams and guttural cries followed by a clenching of the teeth and tautening of all the muscles of the body. It is an impossibility to even move one of her fingers at this time. After an interval of ten minutes, or sometimes longer, there occur great convulsions of the body followed by profuse foaming at the mouth. If attempts to awaken the girl are successful she invariably seems dazed and very often lapses into childish manner of speech—sometimes half weeping—babbling some nonsense—repeating some word or sentence. Twice she has played with her toes and wept when I forced her to stop. Sometimes it takes more than half an hour to persuade her to lie down and sleep after a seizure. The day following she invariably has a dull nervous headache which lessens as the day goes on. The second day following is usually her strongest, brightest day. Nightmares occur on the average of once a week, but sometimes there are three, and rarely more than one in a night."

In addition to the nocturnal crises and the myoclonus, another group of symptoms has been observed, viz., a certain awkwardness or inco-ordination of movement. It is difficult to place the exact time of the appearance of these symptoms, for the reason that the night crises and myoclonia have dominated the clinical picture. It is quite certain however that they have been in existence for the two years, gradually growing more severe. (The mother states that even before the appearance of the nocturnal seizures the movements of the extremities were somewhat clumsy and awkward, and this was especially noticeable in her table manners. This clumsiness was not taken seriously at the time and was regarded simply as a peculiarity of childhood, which would pass off in the course of time.) There is a certain awkwardness in walking and a tendency to balancing on rising from a sitting posture. There is an awkwardness and uncertainty in the use of the arms and hands and a thickness and uncertainty of articulation.

Mentally she is bright and intelligent, but memory is not so good as formerly, and she is at times peevish and irritable, especially on the bad days

when the myoclonia is exaggerated. She is subject to headaches after the nocturnal crises, but not at other times, and is in good general health.

Physical examination.—She is well developed, of average height and muscular development. Seated in a chair and while conversing certain of the muscles of the face, trunk or arms will exhibit a quick muscular contraction, producing a marked locomotor effect. During the interval between these moments of myoclonia her expression and posture are perfectly normal. The myoclonic jerks are frequently initiated by a voluntary movement, such as reaching for some object, an effort to speak or a movement of the head. Usually there is a single jump or jerk and then rest. Occasionally a series of such movements occur and the trunk or limbs are thrown about in a rather bizarre manner.

The pupils are equal and react to light and accommodation. There is no nystagmus. The optic nerves are normal. All of the motor cranial nerves are normal. The articulation is slow, jerky and uncertain. In addition to occasional myoclonic speech disturbance there is slight dysarthria of cerebellar quality.

The upper extremities are normal in their gross motor power and there is no tremor of the outstretched hands. There is however a slight ataxia on the finger-nose test, and a distinct tendency to dysmetria and a very typical dysdiadokokinesis of both arms and fingers. There is also slight hypotonia of the musculature. The Stewart-Holmes sign of hypotonia is absent.

On arising from a sitting posture there is a certain static ataxia and a tendency to balance the trunk. In walking the legs are spread somewhat and there is a moderate degree of cerebellar disorder of progression which is especially obvious on turning corners or turning round suddenly.

In the recumbent posture the heel-knee test shows a moderate degree of dysmetria. There is however no obvious hypotonia. On elevating both arms and legs in the recumbent posture, with the eyes closed, there is no ataxia.

The tendon reflexes of both upper and lower extremities are present and equal on the two sides, viz., the supinator, biceps, triceps, knee jerks and Achilles jerks. Sensation, both superficial and deep, is normal. The spinal column is of normal contour and there is no deformity of the feet. The heart and lungs are normal. Abdomen is normal on palpation and percussion. There is no enlargement of the liver. There is no pigmentation of the skin or cornea. Urine shows no abnormality.

Comment.—The case is of interest as representing a somewhat earlier stage of the dyssynergia cerebellaris myoclonica. Here again there is no family history of myoclonus-epilepsy or of a cerebellar disorder.

Remarks.—The association of cerebellar dyssynergia and myoclonus-epilepsy in this group of cases suggests the occurrence of two independent nervous disorders in one individual. Combined forms of the various congenital, familial and hereditary types of nervous disease are

by no means uncommon, and these associations are especially frequent in the spinal and cerebellar groups of system diseases. For example, Jendrassik [14], who has devoted particular attention to this subject, records many such combinations. He mentions a combined form of Friedreich's ataxia and muscular dystrophy, of spino-cerebellar ataxia and muscular dystrophy, and of Friedreich's ataxia with Huntington's chorea. He also cites the occurrence of myoclonus in association with optic atrophy. André-Thomas [3] has also described a combined form of olivo-ponto-cerebellar atrophy and spinal ataxia.

Such combinations, however, are rare, and show merely a predisposition to the two disorders in the same individual, and would not necessarily indicate any essential relationship between them.

On the other hand, little is known at the present time of the pathology and localization of myoclonus. Its occurrence, therefore, in conjunction with a special type of cerebellar disease, is not without interest, and may have a deeper pathological significance than would appear.

Sioli [19], in a histological study of one of Rechtenwald's cases of myoclonus-epilepsy, found rather widely disseminated histological changes.

In the cerebellum there were enormous collections of lipoid material in the region of the corpus dentatum in the white matter of the cerebellar hemispheres and in the pons. There was also a considerable increase in the number of glia cells. The cells of the corpus dentatum were normal. In the cerebral cortex there was also an excessive deposit of lipoid material in the ganglion cells and glia. The glia cells and fibres were increased in the marginal layer. The cortical changes were all more conspicuous in the region of the central convolutions. The only alteration noted in the spinal cord was atrophy of Hellweg's triangular bundle (olivo-spinal tract).

In the present state of our knowledge, while these two disorders may be regarded as independent manifestations of two distinct disorders in the same individual, the possibility of a closer pathological association should be borne in mind, and the cerebellar mechanism should be carefully considered, both clinically and pathologically, in all cases of so-called myoclonus-epilepsy.

Chapter III.—Dyssynergia Cerebellaris Myoclonica, associated with Friedreich's Ataxia.

Clinical Report of Two Cases, One with Histological Study of the Central Nervous System.

In the previous chapter there was described a group of cases, characterized by progressive dyssynergy, associated with myoclonus-epilepsy. In none of these cases was there any history of an hereditary or familial tendency to either disorder.

In the present chapter I shall present another group of cases in which myoclonus-epilepsy and dyssynergia cerebellaris progressiva were associated with symptoms of Friedreich's ataxia. It is well known that the various cerebellar atrophies and degenerations are not infrequently associated with evidence of spinal cord involvement. Friedreich's hereditary spinal ataxia and Marie's so-called hereditary cerebellar ataxia are classical examples of this association, and may exist alone or in combination. The progressive cerebellar dyssynergia is apparently no exception to this rule—it may exist alone or in combination with spinal cord involvement of the Friedreich's type.

Case 5.

Summary.—A man, aged 36, with symptoms of myoclonus-epilepsy since his twenty-first year. Previous to this there were symptoms of Friedreich's ataxia and progressive cerebellar tremor, which steadily progressed. Pathological study shows the typical spinal lesions of Friedreich's ataxia associated with a primary atrophy of the efferent dentate system of the cerebellum, viz.: considerable diminution in number and extensive atrophy of the cells of the dentate nucleus, with secondary atrophic changes in the superior cerebellar peduncles.

The patient, a man, aged 36, single, was admitted to my service at the Montefiore Home and Hospital on April 15, 1918.

Family history.—His father is living and well. Mother died at 51 from heart disease. The parents were not related. One brother died at age of 2 from pneumonia. He has two other brothers and one sister living and in good health. There is no history of tuberculosis, diabetes, epilepsy, or other nervous disease in the family, with the exception of a twin brother who is suffering from the same malady, and whose case will be presently described.

Previous history.—Had measles in childhood. Was always moderate in the use of alcohol, coffee, and tea. Smoked cigarettes in moderation. Denies venereal infection. No history of trauma.

Present illness.—Began fifteen years ago with attacks of unconsciousness

and convulsive seizures. Patient believes these attacks were caused by fright following a burn. At the time of the accident he was incapacitated for some weeks. The epileptic seizures increased in frequency, and he sometimes fainted on the street and was carried home. A few months later there appeared coarse jerky movements of the extremities. The myoclonus jerks or starts came on gradually and steadily increased in severity and extent.

Even in the earlier juvenile period it was noticed that his manner of walking was awkward and uncertain, and this steadily increased. For the past ten years walking has been unsteady and difficult, speech has been slow and there has also been some uncertainty in the use of the hands. He thinks that part of his inability to walk is due to the fear of falling on account of the myoclonic jerks and starts, which develop on making the slightest effort.

For the past seven years his speech has been quite indistinct and for about the same period of time he has had a marked volitional tremor of the hands on attempting to grasp an object. For three or four years he has suffered from very extreme weakness and unsteadiness of lower extremities and is unable to walk.

During the whole course of the disease there have been no subjective sensory disorders, such as pains or paræsthesias, and there has been no difficulty with the control of the sphincters of the rectum or bladder. States that he has not suffered from headache. He now wears dark glasses constantly, because any bright light increases the tendency to myoclonia. Hearing is not impaired. There are slight evidences of mental impairment and deterioration. His memory is poor, and his mental processes slow. He is querulous, irritable and easily excited.

Physical examination.—Patient is confined to a wheel chair, and is unable to stand or walk without assistance. He wears dark glasses and always seeks a quiet corner of the ward where there is no noise and no excitement. The slightest muscular effort brings on a series of severe myoclonic jerks or spasms which throw him brusquely to and fro in his chair or bed. Talking has the some effect as have also noises or any excitement. As a result of these continuous motor shocks the patient shuns conversation and any social contact. He wishes to be left alone and in quiet.

His speech is slow and typically scanning, and at times uneven and explosive. It is often interrupted by myoclonic jerks and starts in the trunk and extremities, causing sudden shock-like movement. His head is frequently thrown backwards in sharp retro-colic clonus, associated with quick flexor movements of extremities. This larger myoclonic phenomenon is frequently repeated during the course of the examination. Occasional facial grimaces of myoclonic type are also noted. These movements are all accentuated by speech and voluntary movement. The clonic movements are said to occasionally persist in sleep, although in much diminished form. There is a typical and very marked intention tremor of both upper extremities which is associated with dysmetria and dysdiadokokinesis. On attempting to carry the finger tip to the nose the hand is thrown into a violent ataxic tremor similar to

that observed in an advanced case of multiple sclerosis. All tremor movement of the arm immediately ceases in a relaxed or recumbent posture. There are, however, occasional myoclonic starts at rest, which are increased by some one entering the examination-room suddenly. The musculature of the arms is hypotonic and the Stewart-Holmes sign of hypotonia is present in both upper extremities.

Asthenia is present in both arms, viz., when the attempt is made to extend the arm from the body in abduction and maintain the abductive extremity in this position. It can be maintained for a very brief period only, the arm falling to the side, a symptom which may be observed in the intention tremor of multiple sclerosis (asthenia or astasia).

The arm jerks are difficult to elicit and the supinator, biceps and triceps jerks are not definitely present. The abdominal reflexes are not elicitable. The cremasteric reflexes are present on both sides. The plantar reflexes are present but diminished and of the flexor type (no Babinski).

The movements of the lower extremities are extremely ataxic, but in addition to this there is on performing the heel-knee test a very marked intention tremor of both lower extremities. The legs are markedly hypotonic. The knee jerks are absent and the Achilles jerks cannot be elicited. He can stand and walk only with assistance. The Romberg symptom, owing to the extreme ataxia, cannot be tested. In walking, the legs are lifted high and thrown outward in a very ataxic and uncertain manner and resemble the gait of advanced locomotor ataxia. There is no definite spinal curvature but a tendency to pes cavus is present. There is general emaciation and wasting of the musculature but no localized degenerative atrophies.

Sensation.—There is a marked disturbance of the deep sensibility of the lower extremities, and loss of the sense of position. The deep sensibility of the hands is also affected and there is a loss of the sense of position in the hands and fingers. The superficial sensibility to touch, pain and temperature is diminished over the more distal portion of the lower extremities, but is nowhere abolished. The superficial sensation of the upper extremities is fairly well preserved: the only change being diminished acuity of perception over their distal portion. Myotatic irritability of the muscles is active and somewhat increased.

The pupils are equal and react to light and accommodation. Ocular excursions are normal. There is no nystagmus. Hearing is normal. The tongue is protruded in the median line; no atrophy and no tremor. Innervation of the palate is normal. The pharyngeal reflex is active. Facial innervation is normal as well as that of the muscles of mastication. Jaw jerk is not elicitable. The ophthalmological examination by Dr. Tenner revealed no abnormalities. The fundi were negative.

The heart and lungs are negative. Systolic blood pressure 110, diastolic 70. Wassermann test of blood negative. There are no pigmentary deposits of the skin or sclero-corneal margin.

Since his admission to the hospital patient has had very active myoclonia,

The head is thrown suddenly backward, the face is convulsed with occasional myoclonic waves, the arms flex and jerk, the trunk is thrown forward and the legs are flexed and tossed about in a wild and random manner. There are one or two discharges and then a period of rest, although these rest intervals are of very short duration. It is necessary to bind patient with a sheet to the chair, otherwise he would be thrown out, and even with this precaution the wheel-chair rolls around in a wild and reckless manner. This condition is very much aggravated by removal of the dark glasses and the excitement of any examination. Any visit or conversation induces an extreme degree of myoclonia. This condition gradually grew worse, the patient dying of exhaustion a few weeks later.

Comments.—This case differs from those described in the previous chapter in two respects, viz.: the association with Friedreich's ataxia and the familial incidence, a twin brother suffering from the same disease. The first symptoms of the cerebello-spinal disorder made their appearance in the early juvenile period. The myoclonus-epilepsy did not become manifest until the twenty-first year. The presence of the spinal symptoms of Friedreich's ataxia would mask many of the typical symptoms of cerebellar disease. The existence, however, of marked intention tremors and the scanning speech show very clearly the existence of cerebellar involvement (cerebellar tremor) and this was amply confirmed by histological examination.

The central nervous system was subjected to careful histological examination, and revealed the typical spinal lesion of Friedreich's ataxia, together with primary atrophy of the efferent dentate system of the cerebellum, viz.: diminution in number and atrophy of the dentate nucleus with atrophy of the superior cerebellar peduncles. (See report of histological examination.)

CASE 6.

Summary.—A man, aged 29 years, the twin-brother of Case 5. Symptoms of dyssynergia cerebellaris and Friedreich's ataxia for the past ten years, gradually increasing in severity. Myoclonia made its appearance five years ago and epilepsy is only of three years duration.

History.—Patient is 29 years of age, the twin-brother of the case just described. He assists his father in business, who is a tailor by occupation. He resembles very closely his twin-brother in face and stature, and states that he has had symptoms of the same disorder for the past ten years or more. Before that he could run and do anything that other boys were able to do. The condition has been very slowly progressive.

It is characterized by thickness of speech, ataxia and intention tremor of the hands and arms, a certain awkwardness of the movements of walking and running and the symptoms of myoclonus epilepsy. At times there is a lateral tremor movement of the head.

For the past five years he has been subject to nervous shocks or starts, which at first occurred only three or four times a day, but have steadily increased in frequency and intensity. These attacks of myoclonus may

occur spontaneously but more frequently accompany attempts at voluntary movement. They have never approximated in severity those occurring in his brother's case. *Efforts to talk are frequently accompanied by clonic "starts" and "jumps"* (myoclonus), usually only a single movement which may involve the arms, face, neck, trunk and sometimes the legs.

Three years ago he had his first epileptic seizure. At first these attacks were infrequent but have gradually increased in frequency and during the past year have occurred as often as twice a week. In the seizures he is momentarily unconscious and falls to the ground. The obscuration of consciousness is, however, of very short duration. It is as if his legs give way under him, and a darkness comes over his eyes, but he gets up immediately and goes on with what he was doing. There is no biting of the tongue, vomiting, or incontinence of the sphincters, and so far as could be learned no convulsive manifestations. This is a type of seizure which I have referred to the static or posture system of motility—static epilepsy. It is characterized by a sudden loss of control of the static or posture mechanism of standing with transitory obscuration of consciousness and without the usual convulsive manifestations of epilepsy. During the past few years his memory is not so good. There is no history of headache or diplopia, and the special senses are unimpaired. There is no vertigo; no tinnitus aurium; no attacks of nausea or vomiting.

Physical examination (April 28, 1918).—He is of medium height, slenderly built, and bears a very strong resemblance to his twin-brother. The pupils are equal and respond promptly to light and accommodation. The ocular excursions are normal and there is no nystagmus. Motor innervations of the face, tongue, soft palate and muscles of mastication are normal. The fundi are negative. At times, in certain positions a lateral tremor of the head develops.

The speech is dysarthric; rather slow and scanning and at times of a slightly explosive quality. The tongue is protruded in the median line; there is no atrophy or tremor and the palatal innervation is normal. The jaw jerk is not elicitable. Efforts to speak are often accompanied by mild clonic starts or jumps, usually, only a single one, which may involve the face, neck, arms, trunk and sometimes the legs. The station shows a slight unsteadiness but there is no special increase in this slight disorder of equilibrium on closure of the eyes. There is slight awkwardness in walking, especially on coming to a sudden stop or on turning corners. There is a moderate scoliosis in the mid-dorsal region, with a slight convexity towards the left. There is no muscular atrophy of the trunk, arms or legs and no fibrillary twitching. There is no deformity of the feet (no pes cavus). The gross motor power of the arms is normal. The movements, however, are awkward and ataxic and on attempting to carry out a volitional movement a typical intention tremor develops, which is more marked on the left side. The musculature of the upper extremities is moderately hypotonic and the Stewart-Holmes sign of hypotonia is present. (Handwriting, p. 509.)

The arm jerks cannot be elicited (supinator, biceps or triceps jerks). There is typical adiadokokinesis of both upper extremities. There is no loss of

gross motor power in the lower extremities and no evidence of muscular atrophy. There is a moderate degree of hypotonicity of the musculature and the knee jerks and Achilles jerks are absent. The plantar reflex is of the flexion type (no Babinski). The other skin reflexes, abdominal and cremasteric, are present and equal on the two sides.

On attempting to carry out the heel-knee test there are distinct evidences of dysmetria and of an ataxic disturbance, suggestive of the intention tremor but not so distinct as in the upper extremity.

Sensation appears to be normal. The superficial sensibility to touch, pain and temperature is intact, and the deep sensibility of the toes is well preserved. The muscle pain sense on pressure is well preserved.

Comment.—This case, like that of his brother, presents symptoms of dyssynergia cerebellaris progressiva, myoclonus-epilepsy and Friedreich's ataxia in combination.

According to the history, symptoms of cerebellar tremor and Friedreich's ataxia made their appearance some years after the development of myoclonus or epileptiform seizures. It is interesting to note that the epileptiform seizures correspond to what I have termed the static type of epilepsy, viz., a sudden loss of postural or static control without convulsive manifestations.

That the disorder in which we are interested has also been encountered by other observers is shown by the following extract from a case reported by Boschi [5] as ataxie héréditaire; paramyoclonus multiplex, type Unverricht.

The patient was a man 46 years old, who at the age of 15 was subject to convulsive seizures and myoclonus, associated with a well marked ataxic disorder, which had gradually shown a tendency to progression. There was in addition a very marked familial predisposition to the disease. The grandfather, father, and four brothers were all sufferers from the same malady.

Physical examination shows an ataxia of gait, of the movements of the trunk and of the arms. In both upper extremities there is present an intention

tremor. The speech is slow and dysarthric (bradylalia). The knee jerks are exaggerated and there is clonus. The pupillary reflexes are present but slow. The optic nerves are normal. There is a moderate mental defect and typical myoclonus of the Unverricht type.

The case, which is very briefly recorded, would seem to resemble Cases 5 and 6 of my series: dyssynergia cerebellaris myoclonica with Friedreich's ataxia. It is interesting because of the striking hereditary nature of the malady, which was absent in my series of cases.

Undoubtedly other cases have been observed and recorded, but, with this single exception, I have encountered in the literature no other examples in which myoclonus-epilepsy was observed in conjunction with evidence of a cerebello-spinal disorder.

Pathological Study of Case 5.

Autopsy Report.

The autopsy was performed thirty-eight hours after death, by Dr. J. H. Globus, Pathologist to the Montefiore Home and Hospital. His report is as follows:—

The body was that of a poorly developed male, 160 cm. in length. Skin thin, dry, pale, with several decubitus ulcers over lower sacrum, under the anterior superior spine of ilium and over internal tuberosity of right tibia.

The regional lymph nodes were normal in size and slightly palpable.

External genitalia were undeveloped, otherwise normal.

Scalp was free of hair and mottled with numerous small superficial ulcerations. Rigor mortis had disappeared.

On incising abdominal wall, a very small quantity of subcutaneous fat was found. On opening peritoneal cavity no adhesions; no fluid encountered.

Abdominal viscera were found in normal relation to each other and in normal position. No fluid and no adhesions in thoracic cavity.

Lungs, rather voluminous and collapsed only to slight degree. The pericardial cavity was opened after the removal of a thin layer of fatty thymus, and was found free of fluid and adhesions.

Heart, small sized and contracted; weighs 190 gm.

Length of heart, 9 cm.

Muscle bundles of fair size and consistency and of greyish-brown colour. Sub-epicardial fat decreased in amount. All valves intact and normal in size and thickness.

Lungs: Right weighs 600 gm., voluminous, covered by smooth

glistening moist pleura of dark purple-greyish colour. It is interrupted here and there by accumulation of exogenous pigment. On cut section presents a dark purple surface throughout the three lobes of the lung, markedly increasing in consistency, and with numerous dark brownish patches scattered throughout the surface. On pressure, a frothy pinkish fluid is expressed from the alveoli bronchi. No scars, no calcareous deposits are made out.

Left lung: Weighs 500 gm.; presents a similar picture throughout its lower lobe, which is also markedly congested, showing several small patches of consolidation and permits the escape of a pinkish, sero-sanguineous fluid from the alveoli. The upper lobe of left lung is well aerated, of a bright pink colour, collapsed, showing no pathological changes whatsoever.

Liver: Weighs 1,100 gm.; below average in size; surface covered by thin, glistening capsule of a greyish-yellow colour. Cut surface is of a greyish-cream colour. Consistency markedly reduced, lobulation indistinct. Iodine test negative.

Spleen: Weighs 100 gm., small size capsule, thickened and wrinkled. On cut section surface is of a brownish-red colour. Trabecular and Malpighian corpuscles are distinct.

Kidneys: right weighs 120 gm.; left weighs 110 gm.

Both present similar picture. They are of small size. Capsule strips with ease, leaving a smooth greyish-yellow surface. Consistency markedly diminished. On cut section medulla is of normal size, cortex reduced in amount. Aside from a pale yellow colour, no definite pathological changes.

Adrenals: right rather well preserved; left shows a soft medulla with a congested central vein.

Gastro-intestinal tract: the stomach is normal.

Small intestines are collapsed; mucosa shows several patches of marked congestion, otherwise normal.

Large intestine is filled with greenish fluid, on the removal of which a thickened mucosa with numerous small, deep, clean ulcers scattered throughout the length of the large intestine. The ulcers measure from 3 to 5 mm. in diameter, irregular in outline, rather deep seated, base clean and glistening. They become more numerous in the lower portion of the large intestine.

Pancreas is normal.

Blood-vessels are rather strikingly free of arteriosclerotic changes, very elastic but somewhat reduced in circumference.

Bladder is markedly distended, muscular walls stretched, mucous membrane pale, showing a few petechial hæmorrhages.

Testes are small and soft; tubules easily pulled out of supporting tissue.

Prostate is apparently normal.

Neck organs: Right thyroid is twice the size of left, consistency normal. Three parathyroids measuring 5 mm. in diameter, oval in outline, were removed.

Larynx, normal.

Œsophagus, normal.

Brain is of moderate size, shows no apparent reduction in the prominence of the gyri. Several white opacities are seen in the meninges of the cerebral hemispheres. The vessels of the cortex and circle of Willis are normal.

Spinal cord was found to be of average size. Meninges appeared normal; there was no section evidence of degenerative atrophy in the posterior columns, but no other changes could be made out.

Microscopical examination of the viscera (Dr. J. H. Globus) :—

Lungs: Alveoli are crowded with red blood cells and polymorphonuclear leucocytes. The lining epithelium is desquamated, the blood-vessels in the walls are markedly congested. Bronchial tubes have lost their membrane lining, the lumen filled with desquamated epithelium—polymorphonuclear leucocytes. The wall shows marked congestion of blood-vessels.

The liver is normal.

Spleen: trabeculæ prominent, walls of blood-vessels markedly thickened, Malpighian corpuscles in large numbers, fine size, blood-vessels engorged.

Kidneys, normal.

Pancreas, normal.

Adrenals, normal.

Thyroid: alveoli filled with pink staining colloidal matter. Lining epithelium of alveoli extremely thin. Their cellular structure can hardly be made out.

Spermatic cord, normal.

Prostate: alveoli are few in number, few concretions present.

Colon: several small abscesses opening on the surface of the mucosa are found extending deep into the submucosa.

Skeletal muscles: muscle fibres small in calibre, fragmented striations indistinct, nuclei few in number and pyknotic.

Anatomical Diagnosis.

Hypostatic congestion of lungs, lobular pneumonia, pulmonary œdema, fibrosis of spleen and ulcerative colitis.

Histological Examination of the Central Nervous System.

Blocks of tissue were taken from the cerebral cortex, the cerebellar cortex, the dentate nucleus, and the spinal cord for alcohol fixation and the Nissl method.

The brain and cord were fixed in formalin and various levels removed for cellular stains (toluidin blue, hæmatoxylin eosin). The remainder was then placed in Müller's fluid in preparation for the Weigert-Pal method.

Microscopic sections were prepared in the laboratory of the Montefiore Home and Hospital. The larger Weigert-Pal sections were made in the neurological laboratory of Columbia University, and I am much indebted to Professor Tilney for extending to me the courtesy of the laboratory in the preparation of this work.

Spinal cord: The large multipolar cells of the anterior horns are normal, at the cervical, dorsal and lumbo-sacral levels. The anterior roots are normal. The cells of the columns of Clarke in the dorsal region show signs of atrophy and are diminished in number.

The posterior columns show advanced atrophic change which may be traced from the lower lumbo-sacral levels to the nuclei of Goll and Burdach in the lower portion of the medulla (fig. 1).

The columns of Goll are almost completely atrophic, while those of Burdach show a lesser degree of involvement. The posterior cornua appears somewhat reduced in size. The fibres of Lissauer's tract appear fairly well preserved.

There are marked evidences of atrophy in the lateral columns, corresponding to the ventral and dorsal-cerebellar tracts (direct cerebellar and Gowers' tract). There is a lesser degree of diffuse atrophic change in that portion of the lateral columns corresponding to the crossed pyramidal tracts and the spino-thalamic tracts. In the area occupied by the crossed pyramidal tracts this is not clearly defined and as the Babinski reflex was absent it would seem likely, as suggested by Marie, that these atrophic fibres belong to other non-pyramidal systems. This would seem all the more probable as these slighter evidences of atrophy are limited to the cervical and dorsal regions and are scarcely at all demonstrable at the lumbar levels.

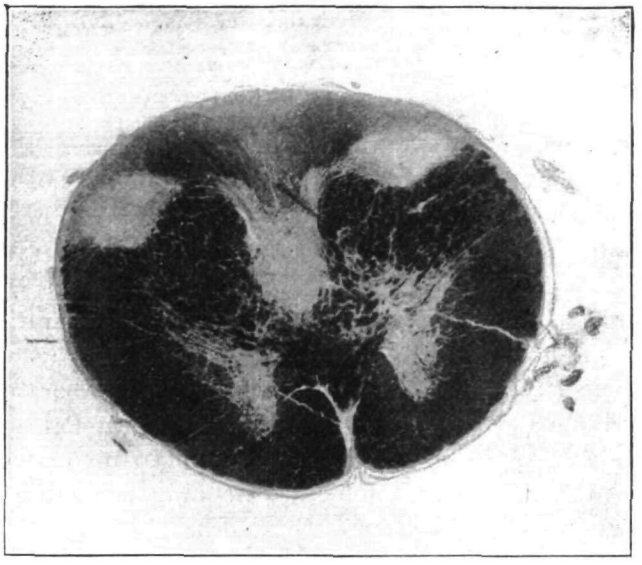


FIG. 1.—Cross section of the medulla oblongata, at the level of the pyramidal decussation. Weigert-Pal stain, showing atrophic changes in the tracts of Goll, Burdach and the spino-cerebellar tracts.

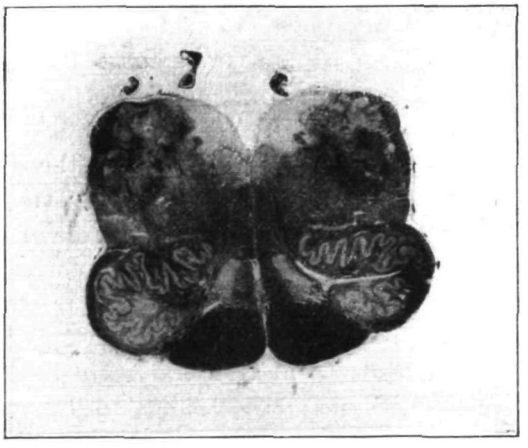


FIG. 2.—Medulla at the level of the inferior olive, showing atrophy of the spino-cerebellar tracts. The pyramidal tracts, the fillet, and the inferior olive and olivo-cerebellar fibres are well preserved.

In the anterior columns there is some marginal pallor, especially in the region of Helweg's tract. The direct pyramidal tracts are not atrophic.

The chief evidences of system involvement are therefore confined to the columns of Goll, Burdach, and the ventral and dorsal spino-cerebellar tracts. In both the cervical and dorsal regions there are, however, slight but rather diffuse atrophic changes.

There are no vascular lesions other than slight secondary thickening in the sclerosed areas, and no evidences of inflammatory lesions. The meninges are slightly thickened in the region of the sclerosed tracts but show no acute changes. The posterior roots show evidences of atrophy. The anterior roots are well preserved.

There is a combined degenerative atrophy of the postero-lateral columns of the cord. Fairly complete of the column of Goll, partial of the column of Burdach; and also of the direct cerebellar tract, Gowers' tract and of the columns of Clarke (cells and fibres). In addition to this there were slight diffuse atrophic changes in the lateral columns. The pyramidal tracts were not atrophic, which is supported by the clinical findings (absence of the Babinski reflex).

Medulla oblongata (fig. 2).—The cranial nerve nuclei of this region (12, 10, 9 and 8) are normal. The pyramids are of normal size and configuration, and there is no evidence of pallor in the Weigert-Pal specimens. The fillet is also normal in size and appearance. The direct cerebellar tracts show atrophic changes as they pass into the corpora restiforme.

The nuclei of Goll and Burdach as well as the fibræ arcuatæ internæ are well preserved.

The inferior olives and accessory olives are normal in size, general appearance and cellular content. The olivo-cerebellar fibres are well preserved.

The descending roots of the trigeminus and the solitary fasciculus are not atrophic.

The fasciculus longitudinalis posticus is normal.

The only noteworthy pathological alterations in this region are the evidences of atrophy posteriorly in the lower levels of the medulla where the tracts of Goll and Burdach pass into their respective nuclei and laterally correspond to the direct cerebellar tracts.

The large sensory and motor projection systems and the inferior olivary complex and its fibres of communication with the cerebellum are normal.

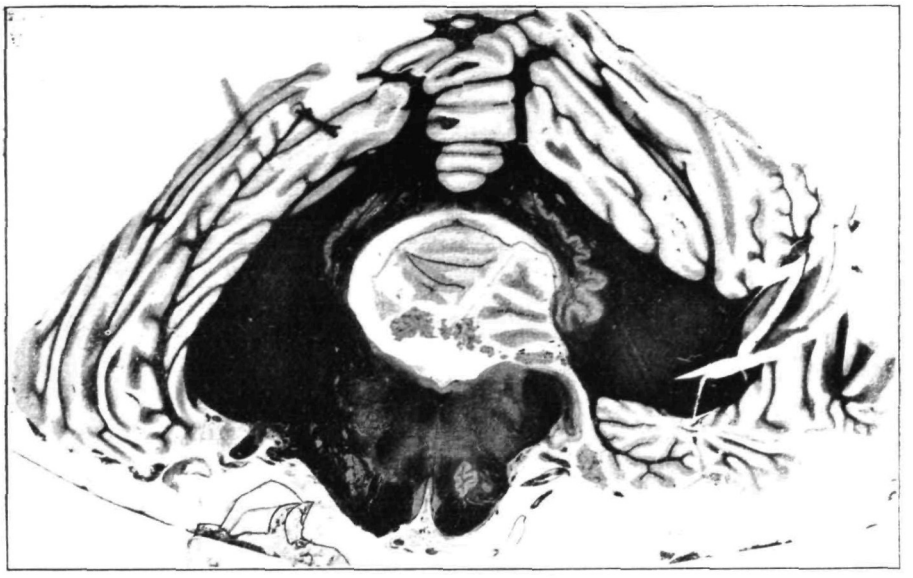


FIG. 3.—Vertical section through cerebellum and pons, at the level of the intrinsic cerebellar nuclei. The peduncles and arbor vitæ of the cerebellum are well preserved.

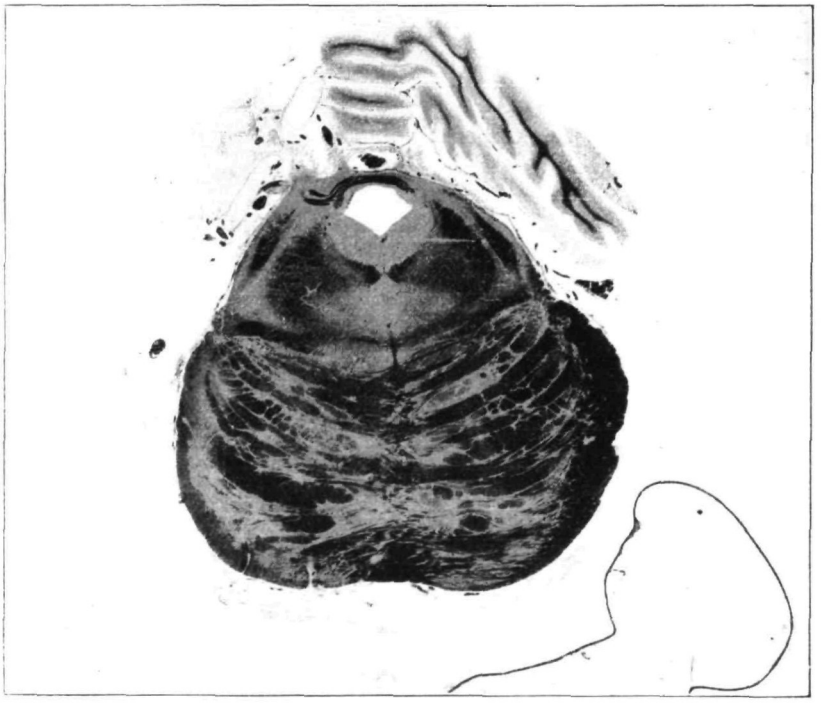


FIG. 4.—Cross section through the pons at the level of the trochlear decussation. Note the marked reduction in the fibres of the superior cerebellar peduncles and especially the atrophic changes in the region of the peduncular decussation. The pontine fibres constituting the stratum superficiale and the stratum profundum are well preserved.

Pons varoli (figs. 3 and 4).—The pontine nuclei, both ventral and dorsal groups, are normal and show no reduction in size or number of the cells. The fibres of the stratum superficiale pontis and the stratum profundum pontis and their continuation in the middle cerebellar peduncles are free from atrophic changes.

The corpora trapezoidii and the superior olives are normal. In higher levels of this region the superior cerebellar peduncles show distinct evidences of atrophy and considerable reduction in size. There are also atrophy and evidences of a marked diminution in the number of fibres at the decussation of the superior cerebellar peduncles.

The cranial nerve nuclei of this region are normal (eighth, seventh, sixth and fifth nerves).

The lateral fillet is normal and the fasciculus longitudinalis posticus is well developed on both sides. The essential pathological change in the pons is an atrophy of the superior cerebellar peduncles. The other structures of the pons, including its peduncles and the pontine nuclei, are normal in size and appearance.

Mid-brain (figs. 5 and 6).—This region reveals the atrophy of the fibres of the superior cerebellar peduncles by the diminished decussation of the peduncles which is so characteristic a feature of these levels. The lateral lemniscus and both anterior and posterior colliculi are normal in appearance.

In the higher levels the ventral decussation of Forel appears apparently in full strength; so while there is a distinct and well-marked atrophy of the fibres passing between the dentate nucleus and the red nucleus this is apparently not continued over into the rubro-spinal tract, which receives further confirmation by the preservation of the cells of the red nucleus.

The various oculo-motor nuclei and root fibres are normal. The cells of the locus niger and of the nucleus ruber appear normal and so far as could be determined there was no reduction in their size or number. Especially interesting is the normal condition of the long projection tracts of the crus cerebri, viz., the fronto-ponto-cerebellar, the pyramidal and parieto-temporo-occipito-cerebellar tracts. The ponto-cerebellar tracts show no evidences whatever of atrophy or pallor.

The only noteworthy change in the mid-brain was the well-marked atrophy of the fibres which enter into the decussation of the superior cerebellar peduncles. I would also emphasize the normal appearance of the connections between the cerebrum and the cerebellum, viz., the fronto-ponto and the parieto-temporo-occipito-ponto cerebellar tracts.

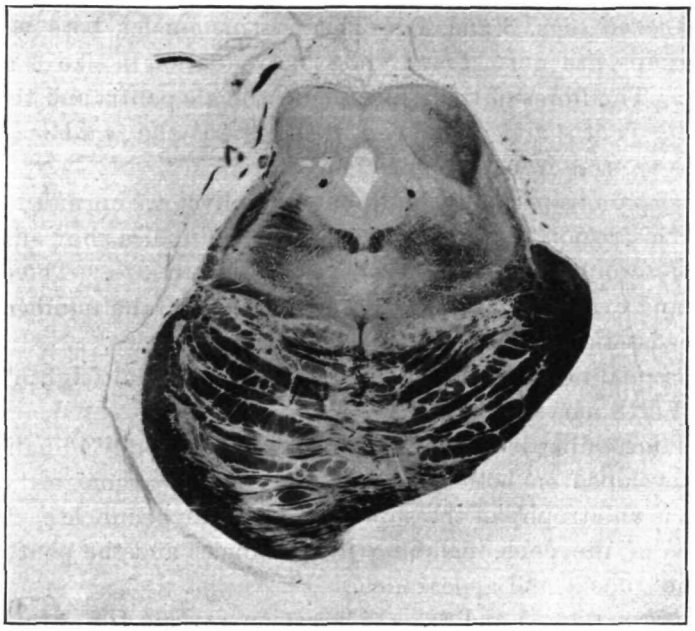


FIG. 5.—Cross section through the inferior corpora quadrigemina, at the level of transition from pons to midbrain. Note the marked reduction in size and the atrophic changes in the region of the superior cerebellar peduncles and their decussation. The stratum superficiale and stratum profundum of the pons are well preserved.

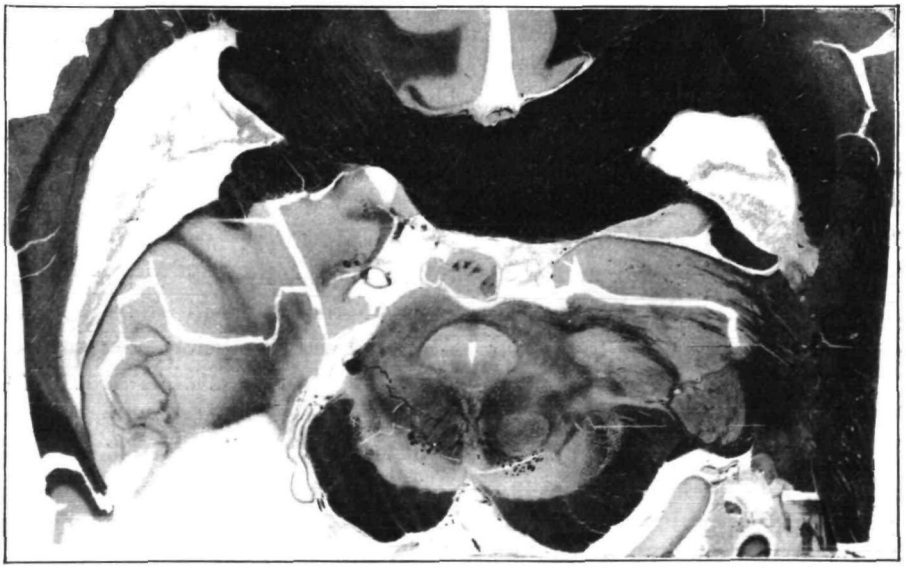


FIG. 6.—Cross section through the superior corpora quadrigemina. The long projection fibres of the crura cerebri are well preserved, including the fronto-cerebellar and the parieto-temporo-occipito-cerebellar tracts. Note diminution of peduncular fibres in the region of the red nucleus.

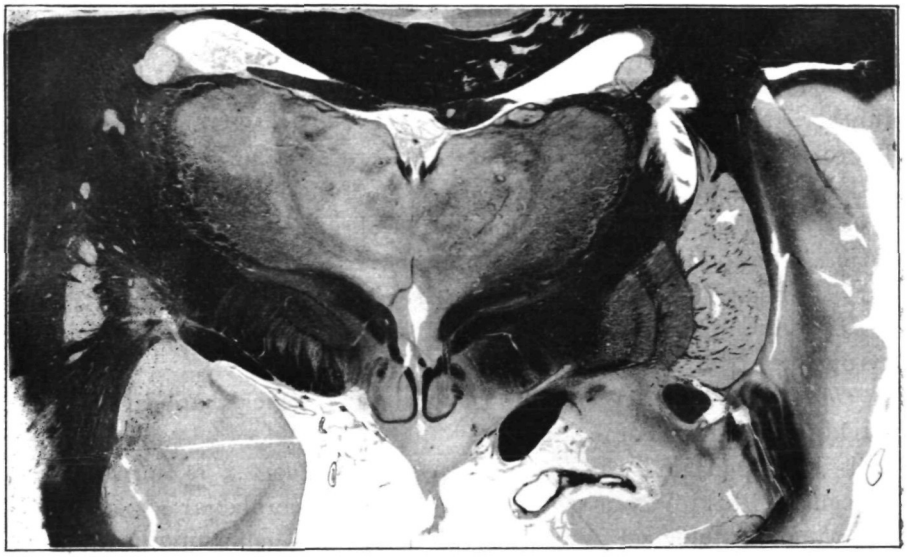


FIG. 7.—Cross section through the interbrain showing the corpus striatum and optic thalamus.

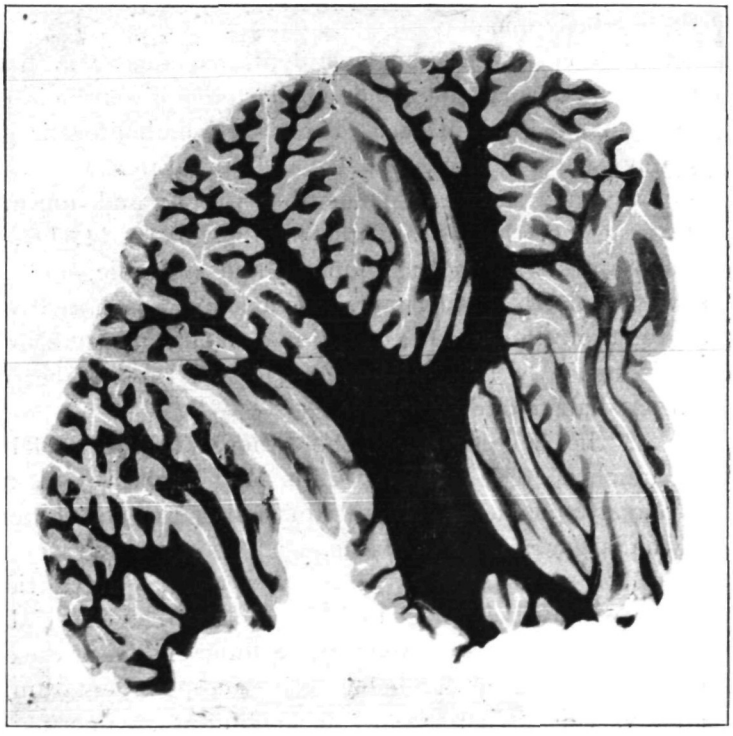


FIG. 8.—Section through the cerebellar hemisphere showing normal arbor vitæ and cerebellar cortex.

Interbrain (fig. 7).—Sections of the interbrain reveal no abnormalities of the optic thalamus or of the corpus striatum. The cells of the locus niger and nucleus ruber are well preserved and are normal in number and appearance as are those of the corpus subthalamicum. There is no apparent atrophy of the fibre systems of either the optic thalamus or corpus striatum.

Cerebral cortex.—Sections of the cerebral cortex from the frontal, parietal, temporal and occipital areas were examined by cellular and fibre stains and revealed no noteworthy abnormality.

The meninges and blood-vessels showed no special pathological changes.

Cerebellum (fig. 8).—The general histological appearance and markings of the cerebellum are quite normal. The arbor vitæ is well developed and the grey matter of the cortex is normal. The molecular, Purkinje, and granular layers of the cerebellar cortex present a normal histological appearance. The large cells of Purkinje are normal in size and number.

Vertical sections were made through the cerebellum including the structures of the pons and medulla oblongata. In these sections were included the intrinsic nuclei of the cerebellum.

The convolutions of the nucleus dentatus appear a little less voluminous than is normal and the cerebellar olive gives the impression of being somewhat reduced in size. The nucleus emboliformis, globosus and tecti are present and of normal size and appearance.

Histological study shows a considerable atrophy and diminution in number of the cells of the dentate nucleus (figs. 9, 10, 11, 12). Many of these cells appear shrunken, rounded and atrophic, and a large number have completely disappeared. An attempt was made to estimate in some degree the cellular loss by making comparative cell counts with normal specimens. By this method the loss in the number of cells varied from one-half to one-third.

Because of the small size of the other intrinsic nuclei of the cerebellum (nucleus tecti, emboliformis and globosus) it was not possible to make the same accurate estimation of the cell content as in the case of the larger nucleus dentatus.

A study of the sections, however, revealed little, if any, evidence of cellular loss or atrophy. The cells of the nucleus tecti especially were numerous and well preserved. The chief cellular changes were confined to the convolutions of the cerebellar olive (corpus dentatum). The meninges and vascular structures of the cerebellum were normal. Only

within the nucleus dentatum did the blood-vessels show some secondary thickening.

The cerebellum was, therefore, normal in its histological appearance, with the sole exception of an extensive and well-marked atrophy of the cells of the dentate nucleus.

FIG. 9.—Dyssynergia cerebellaris myoclonica. Primary atrophy of the dentate system. Hæmatoxylin-eosin stain, section of the corpus dentatum, showing the convolution of the cerebellar olive and the great reduction in size and number of the cells of the corpus dentatum.

Summary of Pathological Changes.

The histological study of the central nervous system in this case showed the typical spinal cord changes of Friedreich's ataxia. There was atrophy of the posterior columns of the cord which could be traced

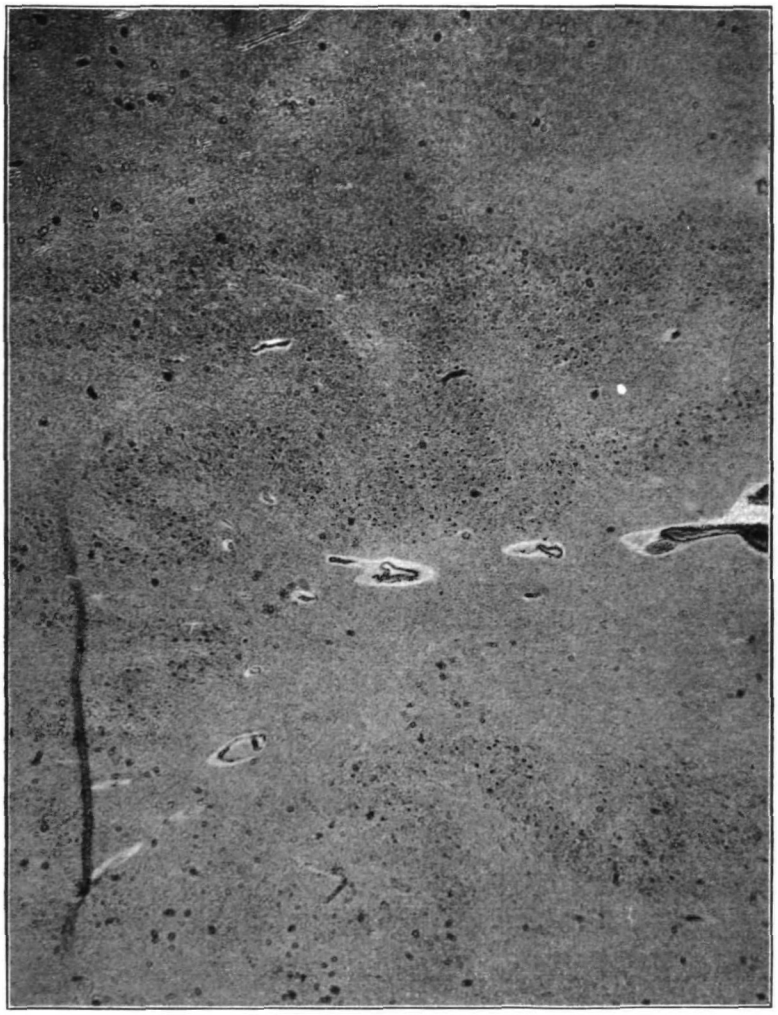


FIG. 10.—Normal control: same magnification and stain as fig. 9. Section through the corpus dentatum, showing convolution of the cerebellar olive and normal appearance of the cells of the corpus dentatum.

to the nuclei of Goll and Burdach in the medulla. Atrophic changes were also present in the direct cerebellar tract of Flechsig and the tract of Gowers (ventral and dorsal spino-cerebellar tracts). The

columns of Clarke were atrophic, and there were also some changes in the area occupied by the spino-thalamic tracts.

There was no definite atrophy of either the direct or crossed pyramidal tracts and the slight pallor in certain areas I would ascribe to

FIG. 11.—Hæmatoxylin-eosin. The corpus dentatum of dyssynergia cerebellaris myoclonica showing marked atrophy and diminution in number of the cells of the cerebellar olive. (Primary atrophy of the dentate system.)

degeneration of other non-pyramidal fibres which belong to this region.

Histological study of the brain-stem and cerebellum showed the

following conditions: There was an extension into the medulla of the system atrophies of the cord, viz., the direct spino-cerebellar tracts. The atrophy of the posterior columns apparently ceased at their ter-

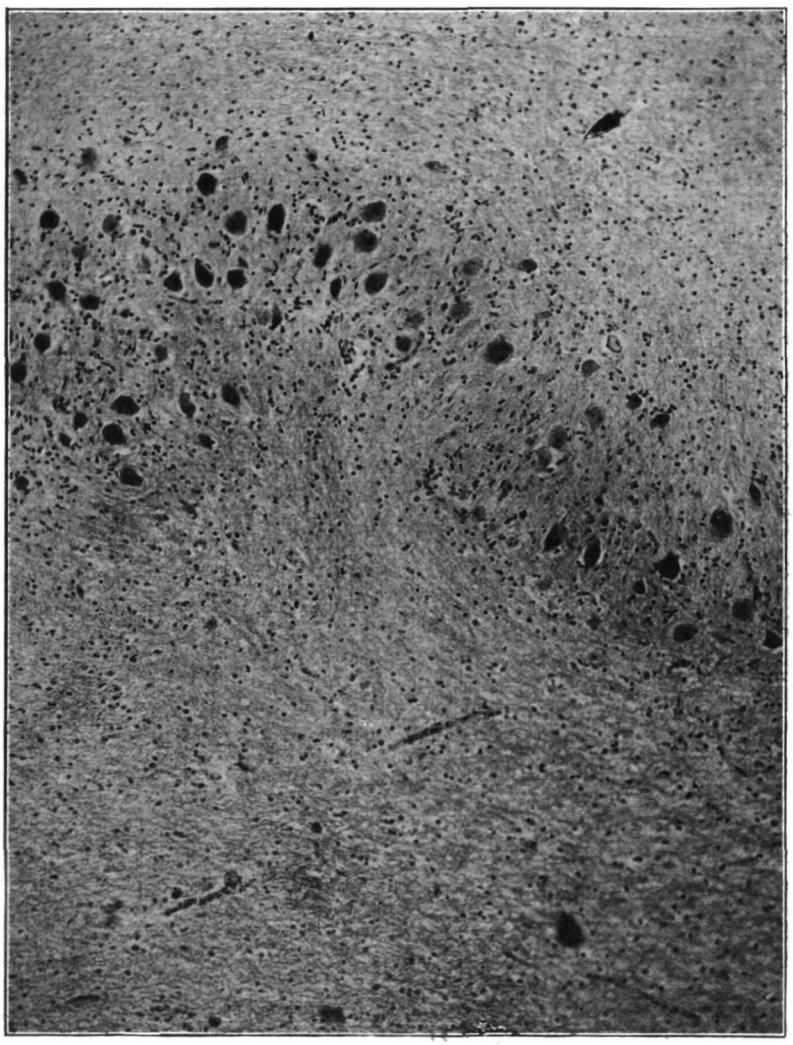


FIG. 12.—Normal control. Same magnification and stain as fig. 11. Showing normal appearance of cells of the corpus dentatum.

mination in the nuclei of Goll and Burdach, for the fibræ arcuatæ internæ were well preserved and the corpus restiforme well developed.

The other important and essential lesion was an atrophy of the

motor cells of the corpus dentatum of the cerebellum and of their efferent neurones in the superior cerebellar peduncles. There was no atrophy of the other cerebellar systems, and none of the nucleus ruber. The lesion was therefore confined to this short and very important internuncial common path which conveys the motor impulses of cerebellar origin to the spinal pathways.

The lesions were therefore both spinal and cerebellar. The spinal lesion is that common to Friedreich's ataxia; the cerebellar lesion I would regard as a special form of system disease, viz., primary atrophy of the efferent dentate system of the cerebellum.

Chapter IV.—Primary Atrophy of the Efferent Dentate System and its Relation to Dyssynergia Cerebellaris Progressiva (Progressive Cerebellar Tremor).

Anatomical Considerations.

The cerebellum is an extremely complex ganglionic structure, having massive and important connections with the spinal cord, brain stem and the cerebrum. It has an elaborate convoluted cortical structure, composed of various cellular and association layers, as well as commissural systems and peduncles. The inferior and middle peduncles are composed of afferent fibres on their way to the cerebellar cortex.

The inferior cerebellar peduncle or corpus restiforme consists of two divisions, a spinal and a bulbar. Among its constituents are the direct cerebellar tract; the anterior and posterior arcuate fibres of the nuclei of Goll and Burdach; olivo-cerebellar fibres; fibres from the nucleus lateralis and nucleus arciformis of the medulla; and the nucleo-cerebellar tracts consisting of fibres passing from the cranial nerve nuclei of the pons and medulla.

The chief constituents of the middle cerebellar peduncle or brachium pontis are: (1) the fronto-ponto-cerebellar tract; (2) the temporo-ponto-cerebellar tract; (3) the occipito-ponto-cerebellar tract; and (4) the parieto-ponto-cerebellar tract. According to Tilney and Riley [6] these fibres originate in cells of the frontal, temporal, occipital and parietal lobes respectively. They descend through the internal capsule and the cerebral peduncle to end in the cells of the pontine nuclei. From these cells arise the ponto-cerebellar fibres which decussate in the pons and pass to the cerebellar hemisphere of the opposite side.

The superior peduncle, on the other hand, is essentially efferent and

motor in function, providing the principal pathway for the distribution of cerebellar impulses to the muscular system.

This system of fibres, together with its fellow of the opposite side, undergoes a complete decussation before reaching the red nucleus of the midbrain. Its chief constituents are the cerebello-rubral tract and the cerebello-thalamic tract. It also contains a cerebello-tegmental tract.

The efferent fibres composing the superior cerebellar peduncle arise in cells of the intrinsic nuclei of the cerebellum. These are the dentate nucleus, the nucleus globosus, the embolus, and the nucleus tecti. Efferent fibres from the nucleus tecti also pass in the juxta-restiform body to the motor cranial nerve nuclei of the brain-stem (cerebello-nuclear fibres). The dentate nucleus is related to the neocerebellum or hemispheric system. Phylogenetically, it coincides in development with the cerebral cortex. The other intrinsic nuclears are older and are related to the paleocerebellum or vermian system.

All of the efferent fibres arising in cells of the intrinsic nuclei I would include under the general heading of the efferent dentate system. Those originating in the paleocerebellar nuclei may be distinguished as the *paleodentate system* and those belonging to the dentate nucleus proper as the *neodentate system.*

This would simplify our existing nomenclature for the various constituents of the efferent cerebellar system (cerebello-rubral, cerebello-thalamic, and cerebello-tegmental system), and is justified by their morphological and functional identity. The term *dentate* is chosen, as the various efferent fibre systems of the cerebellum all take their origin in the intrinsic nuclei of the cerebellum, of which the dentate is the chief constituent. This, the more recent acquisition in the phylogenetic sense, represents the neodentate system, in contra-distinction to the paleodentate system which takes its origin in the older nuclei.

Pathological Considerations.

In Chapter II I have described in some detail a group of cases characterized by symptoms of a progressive cerebellar disorder, associated with myoclonus-epilepsy.

In Chapter III a similar group of cases was reported in association with Friedreich's ataxia. In one of these cases with symptoms of a cerebello-spinal involvement, a careful histological study was made of the central nervous system, with the following results:—

The spinal cord showed the typical lesions of Friedreich's ataxia, which represented the pathological basis for the spinal symptoms of the disorder. A careful examination of the cerebellum and its connections revealed in addition an atrophy of the cells of the dentate nucleus and of the superior peduncles of the cerebellum.

The nature of the atrophic process and the strict limitation of the lesion to a special group of neurones are characteristic of a system disease. This condition I believe is a primary atrophy of the efferent dentate system of the cerebellum, and the cause of the cerebellar portion of the symptomatology.

Atrophic changes in the cells of the dentate nucleus in cases of Friedreich's ataxia have been previously described by Spiller [20], and also by Thomas and Durupt [4], in association with other lesions of this region. In the case recorded by Thomas and Durupt there were in addition to atrophy of the dentate nucleus pathological changes in the red nucleus, the fillet and the posterior corpora quadrigemina.

Like the spinal cord, the cerebellum shows a special tendency to various types of congenital defects and system diseases. These may be limited to the cerebellum but are often combined with spinal cord changes, and represent a group of cerebellum-spinal disorders. Prominent among these are the hereditary spinal ataxia of Friedreich, and the hereditary cerebellar ataxia of Marie, which may be present alone or in combination. In this disorder the lesion of the cerebellum is usually a general atrophy of the whole organ, which appears much reduced in size.

In addition to this more general type of cerebellar atrophy many more circumscribed forms are recognized, in which the lesions are limited to certain special systems of the cerebellar mechanism.

There is, for example, the olivo-ponto-cerebellar atrophy of Dejerine and Thomas [6] in which the atrophic lesions are confined to the inferior olive and its cerebellar connections, the pontine nuclei, middle peduncles of the cerebellum and the cerebellar cortex. All of the intrinsic nuclei of the cerebellum and the superior cerebellar peduncles are intact. This type is neither congenital, hereditary nor familial and appears only in later life.

Then there is a type described by Gordon Holmes [9], the olivo-cerebellar type of cerebellar atrophy. In this form there is atrophy of the cerebellar cortex, the inferior olive and the olivo-cerebellar tract. The pontine nuclei and middle peduncles, and the intrinsic nuclei and superior cerebellar peduncles are normal. This form differs from the preceding in its familial incidence.

Still another type has been added by Le Jonne and Lhermitte [15], the olivo-rubro-cerebellar atrophy. This form is characterized by atrophy of the inferior olive and olivo-cerebellar fibres, but also include the intrinsic nuclei, the superior cerebellar peduncles and the cells of the nucleus ruber. The structure of the cerebellar cortex, the pontine nuclei, and middle peduncles are intact.

The lesions in all of these types are those of simple atrophy which characterize a system-disease, and consist of primary degeneration of the parenchyma with secondary proliferation of glia.

In addition to the cerebellar system diseases there are also pure cortical types of cerebellar atrophy in which the degenerations are limited to the finer structures of cerebellar cortex (cells of Purkinje and granular layer). Such cases have been described by André-Thomas [1] and Rossi [17], and present the typical clinical picture of cerebellar disease.

At the present time we may recognize therefore the following pathological types of cerebellar atrophy. The cerebellar cortical type of André-Thomas, the olivo-ponto-cerebellar type of Dejerine and Thomas; the olivo-cerebellar type of Holmes, and the olivo-rubro-cerebellar type of Le Jonne and Lhermitte.

To these various types I would add the primary atrophy of the dentate system (figs. 9 and 11). This is a system disease characterized by atrophy of the cells of the dentate nucleus (neodentate system) and thinning of the superior cerebellar peduncles. All other important structures of the cerebellum, the cortex, the olivo-cerebellar and ponto-cerebellar systems are intact. In this group of cases the symptoms of a cerebellar disorder are much more evident in the co-ordinated movements of the extremities than in those of the trunk. The cerebellar or intention tremor which was present in greater or lesser degree in all of the cases was a characteristic symptom. The dyssynergia is, therefore, of the appendicular rather than the axial type. In this respect differing from the massive trunkal involvement of many other forms of cerebellar atrophy.

There already exists in medical literature a number of isolated facts tending to show the close connection between, what I term, the dentate system and the cerebellar or intention tremor. The relation of the intention tremor to the cerebello-rubral system was emphasized some years ago by Gordon Holmes [8], based on numerous clinical and pathological observations. Sander [18] and Touche [22] have also reported cases of intention tremor in association with lesions of the

dentate nucleus. In the experimental field, the work of Ferrier and Turner [7] on monkeys has also shown the relation of the cerebellar or intention tremor to the efferent cerebellar system. After section of the superior cerebellar peduncles these investigators observed: "Except when quite at rest, a constant tremor in the homolateral arm and leg which passed into larger oscillation on volitional effort. The limbs were the subjects of fine tremors which became amplified on exertion."

As the pathological changes in the case just recorded are limited to the neodentate system of the cerebellar mechanism, it is but natural that the more recently acquired and more highly differentiated motor activities should show the greatest degree of involvement. It is for this reason I believe that the affection is predominantly appendicular in its manifestations and the intention tremor so conspicuous a symptom, the neodentate portion of the efferent cerebellar system showing a greater vulnerability to abiotrophic degeneration.

In this respect, there is a certain similarity to another system disease which I have described in relation to the corpus striatum, viz., the primary atrophy of the efferent pallidal system [11].

This disease represents a *primary* or *essential* form of paralysis agitans. The pallidal system, like the dentate system, is a common pathway and serves for the transmission of all motor impulses from the corpus striatum. In this form of paralysis agitans the earliest involvement is usually of the extremities, which is probably due to the initial atrophy of the pallidal cells of the neostriatum (neopallidal cells). I believe, therefore, in the cerebellum as well as in the corpus striatum we must recognize the existence of an internuncial common pathway for the transmission of efferent impulses. Both systems may be the seat of abiotrophy in the sense in which this term was used by Gowers. One is the primary atrophy of the pallidal system causing the primary or essential form of paralysis agitans. The other is primary atrophy of the dentate system causing the primary or essential form of dyssynergia cerebellaris progressiva. In addition to these manifestations of primary atrophy, secondary and symptomatic forms may be recognized, caused by tumours, inflammatory and vascular lesions.

Chapter V.—The Relation of the Cerebellum to the Static or Posture System of Motility.

All investigators have recognized the important rôle played by the cerebellum in the control and regulation of motility, its influence on muscle tonus, equilibrium and the co-ordination of movement. The trend of modern opinion, under the leadership of Babinski, has been to group all cerebellar symptoms under the general heading of synergia. According to this conception, which is now generally accepted, the essential function of this important structure is the regulation of the synergies of movement, and synergia is regarded as the principal function of the cerebellum. And yet, notwithstanding this recognized rôle in the control of movement, there is much that the prevailing theories of cerebellar function have failed to explain.

In the course of previous investigations on the subject of motility I reached the conclusion that the efferent nervous system is susceptible of division into two separate components which I termed *the static and kinetic systems* [12] [13]. As this conception has an important bearing on the interpretation of cerebellar symptoms a brief outline of its chief features may be given here.

According to this view, motility is subserved by two distinct components, each represented throughout the entire efferent nervous system by separate neural mechanisms, which are physiologically and anatomically distinct. One is the movement proper, which is subserved by the *kinetic system* (motion system). The other represents that more passive form of contractility which we recognize in tonus, posture and equilibrium and is subserved by the *static system* (posture-system).

The term static is used to designate that peculiar property of the muscle fibre by which it becomes fixed in posture. In the reflex nervous system this is manifested by postural tonus and at the higher levels by various postures and attitudes.

There are many reasons for the assumption that the kinetic system is related to the anisotropic discs and the static system to the sarcoplasm of the muscle fibre, as these elements differ in structure, innervation, mode of contractility and metabolism.

There are also reasons for the assumption that the transformation of movement into posture is effected by fixation of the sarcoplasm which converts the contractile muscle fibre from a kinetic into a static mechanism.

Therefore, movement is subserved by a kinetic, and posture by a

static mechanism, the two systems supplementing one another and working together in harmony. For every movement starts from posture, is accompanied by posture, and terminates in posture, posture following movement like a shadow. At the same time, the postural mechanism exercises a stabilizing influence upon the course of movement itself.

Motility as it is observed in animal life may be divided more or less arbitrarily into three distinct groups, viz., reflex, automatic-associated, and isolated-synergic or dissociated types of movements.

All of these forms of movement are intimately associated with that other component of motility which we term posture, and the same postural groups may be recognized as in the classification of movement, viz., *reflex postures, automatic-associated postures* and *isolated-synergic types of posture* corresponding to their respective motion mechanisms. And it may be stated as a general principle that there is no form of motility from the simple reflex to the most skilled and individualistic type of movement which functions without a corresponding static or posture mechanism.

The essential integrating and correlating mechanism for the control of the static function of motility I believe to be the cerebellum. Afferent impulses from the periphery and efferent impulses from the cerebral cortex pass to this organ before their final distribution by way of the cerebello-spinal system to the posturing or static mechanism of skeletal muscles.

The older cerebellum stands in relation to what may be termed the *paleostatic system* which controls the older static or postural functions of "automatic and associated type." It takes its origin in the older nuclei of the vermis cerebelli (N. fastigii, globosus, emboliformis).

The cerebellar hemispheres, on the other hand, regulate the higher postural functions of motility through the medium of a neostatic system, which takes its origin in the cells of the dentate nucleus. The neostatic system is controlled from the cerebral cortex by special tracts which connect the various regions of the cerebral cortex (frontal, parietal, temporal and occipital) with the dorsal and ventral nuclei of the pons varolii, and thence to the opposite hemisphere of the cerebellum.

In posture, as in movement, no sharp line of demarcation can be drawn between the various types, and one group merges imperceptibly into another.

It is interesting to observe that all posture systems, *neostatic* as well as *paleostatic*, pass to the cerebellum for final integration and

co-ordination. This is in accord with the nature of the posturing mechanism and its secondary and unconscious rôle in motility. For while the higher forms of movement are initiated as conscious and voluntary processes, the corresponding postures are secondary, and follow automatically in the path of movement.

The cerebellum, then, is an organ which is engaged in the control and regulation of the static or *posture synergies* of motility. In it are represented the infracortical centres for the posturing mechanism which are under both spinal and cerebral control. I would, therefore, regard the cerebellum as a central ganglionic station for the co-ordination and control of static or posture synergies—in contradistinction to kinetic or motion synergies which are localized in their respective kinetic spheres (rolandic and striatal). The static synergies are manifestations of the sarcoplasm of the muscle fibre and the kinetic synergies of the anisotropic discs. The static or posture mechanism according to this conception is concerned in the regulation of muscle tonus, the maintenance of postures and attitudes, and is also an important factor in guiding, checking and fixation of movement.

A striking experiment cited by André-Thomas [2], may be mentioned in confirmation of this point of view. A dog whose cerebellum had been removed was unable to stand or walk. When, however, he was thrown into the water he could swim without difficulty. This peculiar phenomenon I would explain as follows: When the animal attempted to stand or walk, the posturing mechanism was essential to co-ordinated movement, to counteract the force of gravity. In a supporting fluid medium like water, however, posture synergies are of secondary importance, and as the kinetic system with its synergies are undisturbed the act of swimming takes place without difficulty.

In many respects, this theory of posture synergy also harmonizes with our modern conception of cerebellar symptomatology. In the co-ordination of all forms of movement, posture synergy is of prime importance. Loss of this control is, I believe, the cause of the scanning speech, cerebellar ataxia, intention tremor, hypermetria, adiadokokinesis and nystagmus which we observe in cerebellar disease.

In cerebellar ataxia, for example, a characteristic feature is the decomposition of movement which takes place during the execution of a co-ordinated act. When this is present it requires several disjointed movements to accomplish what is normally performed as a continuous one. The discontinuity of movement, which is one of the cardinal

symptoms of cerebellar disease, may be referred to a disorder of posture synergy which prevents the posture and motion systems from acting together in harmony. The decomposition of movement represents therefore an effort to compensate for the loss of the posturing mechanism.

Hypermetria and dysmetria of cerebellar origin may also be explained by a failure of the posture system in its function of guiding and checking movement. For in any co-ordinated act, posture formulæ are as necessary as motion formulæ and play an important rôle in giving stability and direction to movement. The checking of movement and its fixation in posture is also an essential function of the static system.

Adiadokokinesis may likewise be ascribed to a disorder of the static mechanism, the rapid succession movements which characterize this disorder being dependent upon quick fixation and sudden release of the posture mechanism.

The cerebellar or intention tremor is a particularly striking example of a disorder of the posture mechanism. When a patient presenting this symptom attempts a movement, the extremity passes into coarse ataxic oscillations which increase in intensity as the object is reached and the extremity tends to become fixed in posture. There is a coarse ataxia and tremor-like oscillation not only during the passage of the movement, but also during attempts at fixation. It is particularly at the end of the movement when the extremity tends to become fixed in posture that the intention tremor is often most active. This characteristic of the intention tremor is due to a posture asynergia, and serves to differentiate it from other forms of purely kinetic ataxia.

Cerebellar nystagmus may also be mentioned as representing a similar mechanism. Here again the movements increase when the attempt is made to fix them in posture.

Very interesting is the influence of the vestibular mechanism on the posture system of skeletal muscles. Barany has shown that all movements, trunkal and appendicular, are under a certain labyrinthine control. This is shown by the nystagmus, the pass-pointing and falling tests.

In brief then, while asynergia may be regarded as the fundamental symptom of cerebellar disease, I would limit this conception to *posture asynergia*, which is a disorder of the static or posture system of motility.

Posture asynergia may be paleostatic or neostatic, depending upon the portion of the cerebellum involved. Paleostatic asynergia is a disorder of lower forms of posture of automatic-associated type, and is largely trunkal or axial in distribution. Neostatic asynergia, on the other hand, is a disorder of the higher forms of posture, of isolated synergic type and is essentially appendicular in distribution. One is a spinal, the other a cerebral form of asynergia.

In the system disease of the cerebellum described in the previous chapter—"Primary Atrophy of the Dentate System"—the atrophic changes were limited to the cells of the corpus dentatum (neodentate system). This is a system which is related to the neocerebellum and its recently acquired functions. For this reason the cerebellar symptoms of this disorder are predominantly appendicular in distribution, the extremities representing in the realm of posture, as in movement, the highest degree of development.

Chapter VI.—Concluding Remarks.

In the previous chapters, under the title, "Dyssynergia Cerebellaris Myoclonica," I have described what appears to be a well-defined type of nervous disease, presenting the clinical picture of a progressive cerebellar disorder in association with myoclonus-epilepsy. Four of the cases were sporadic and no history could be elicited of any hereditary or familial tendency to either cerebellar disease or myoclonus-epilepsy.

The cerebellar disturbance affected more especially the finer movements of the extremities and the dyssynergia was predominantly appendicular in distribution. The cerebellar or intention tremor was a marked feature of all the more advanced cases, in this respect resembling the clinical group which I described some years ago under the title "Dyssynergia Cerebellaris Progressiva," or "Progressive Cerebellar Tremor."

The myoclonus-epilepsy, in its general manifestations, was very similar to the disorder as described by Unverricht [23]. The familial incidence, however, which is one of the chief characteristics of the Unverricht type, was lacking, excepting in the group associated with Friedreich's ataxia. The myoclonus-epilepsy, therefore, resembles in some respects the type of the disorder described by Rabot [16]. This is a sporadic form, beginning somewhat later in life than the Unverricht type and in which the myoclonus is intermittent in character and less

progressive in its evolution. Fundamentally, however, both types are very similar and are united by transition forms.

The relation of the cerebellar disorder to myoclonus-epilepsy in the group of cases which I have described is quite obscure and in the present state of our knowledge but little light can be thrown on this question. It is quite possible that the combination is only accidental and represents the association of two independent nervous disorders in a predisposed individual. Such combinations in the realm of neuropathology are by no means uncommon. Nevertheless, I think that one should not be too hasty in concluding that here is a mere combination of separate clinical entities. We know so little of the underlying cause and pathology of myoclonus and its relation to the various structures of the central nervous system that the possibility of a form related to the static or posture system should be considered. It is conceivable, for example, that sudden breaks in the continuity of postural control or synergy might express themselves in terms of compensatory movements of a myoclonic type.

Interesting in this connection are the peculiar epileptiform attacks which occurred in two of the cases, which I have termed static seizures. These attacks are characterized by sudden loss of postural control without convulsive manifestation and are accompanied by slight transitory obscuration of consciousness. The patient without warning plunges suddenly to the ground, apparently from a sudden cessation of postural control. These attacks are so sudden and the fall so immediate that injury is very likely to ensue. There are no muscular spasms and the patient rises almost immediately. The blurring of consciousness is often only momentary; indeed in some of the attacks consciousness is apparently unaffected.

In addition to the clinical type, termed dyssynergia cerebellaris myoclonica, a similar complex of symptoms was observed in another group of cases associated with the spinal symptoms of Friedreich's ataxia. These, however, were of the family type, two cases occurring in one family. Mention was also made of an observation recorded by Boschi showing that such combinations of symptoms, while rare, are not unknown in medical literature.

In one case, belonging to this group, a careful histological study was made of the central nervous system, which revealed the typical spinal lesions of Friedreich's ataxia, in conjunction with a peculiar type of system atrophy of the cerebellum, which I termed primary atrophy of the dentate system. The atrophic changes involved only the cells of the

corpus dentatum and the fibres of the superior cerebellar peduncles. The pathological changes were therefore limited to the cells and fibres of a special system of neurones, which because of their relation to the dentate nucleus was termed the dentate system. All other structures of the cerebellum were normal.

To the other recognized system atrophies of the cerebellum, viz. : the cerebellar cortical atrophy, the olivo-ponto-cerebellar atrophy; the olivo-cerebellar atrophy and the olivo-rubro-cerebellar atrophy, I would add the atrophy of the dentate system, which is a primary atrophy of its chief efferent system. The association of this form of cerebellar atrophy with Friedreich's ataxia is not surprising in view of the frequency of cerebello-spinal combinations.

The cerebellar portion of the symptomatology of dyssynergia cerebellaris myoclonica I would refer to the atrophy of the efferent dentate system. In the present state of our knowledge it is difficult, if not impossible, to refer general cerebellar symptoms to special parts of the cerebellar mechanism. And it is generally held that the various types of cerebellar atrophies mentioned above cannot be distinguished with certainty on the basis of their cerebellar symptomatology alone. In other words, asynergia is the characteristic symptom of cerebellar disease, no matter which portion of the cerebellar mechanism is involved.

It is, therefore, with some hesitation that I suggest the early appearance and predominance of appendicular asynergia and especially the cerebellar tremor as perhaps characteristic of this type of cerebellar disease (primary atrophy of the dentate system) and yet these were the characteristic features of the clinical type under consideration.

Some years ago I described a primary system disease of the corpus striatum which was associated with the symptomatology of paralysis agitans. The lesions consisted of atrophy of the large motor or pallidal cells of the corpus striatum, and of their efferent fibres in the ansa system. The disorder was called primary atrophy of the pallidal system. This I regarded as the primary and essential form of paralysis agitans and all other clinical manifestations of the disease as secondary or symptomatic in nature due to vascular, inflammatory and neoplastic lesions.

A similar differentiation may be made in the case of the cerebellum and its efferent pathway, the dentate system. This may be the seat of a primary atrophic process producing the characteristics of a cerebellar disorder (primary atrophy of the dentate system). This system may

also be the seat of secondary or symptomatic involvement from tumours, inflammations and vascular lesions. The intention tremor of multiple sclerosis is a symptomatic manifestation of involvement of this system.

Primary atrophy of the pallidal system is, therefore, a disorder of a kinetic mechanism, giving rise to the symptomatology of paralysis agitans. Primary atrophy of the dentate system is a disorder of a static mechanism, giving rise to the symptomatology of dyssynergia cerebellaris.

In the final chapter I presented my views on the functions of the cerebellum and its relation to the static system of motility. According to this conception the function of the cerebellum is the control of the posture synergies of movement. Motility is subserved by two components throughout the whole of the efferent system, a kinetic or motion system and a static or posture system, both working together in harmony.

Motility, operating through its contractile mechanism, is therefore a compound of movements and postures. Movement is the active component which propels the organism or parts of the organism in space, the peripheral contractile mechanism of which is represented in the anisotropic discs of the striated muscle fibre. Posture is that more passive component which is represented in tonus and attitude. It tends to counteract the forces of gravity and the effects of atmospheric pressure and maintains the organism in a state of static equilibrium. The peripheral organ of this mechanism is the sarcoplasm of the muscle fibre. This system also plays an important rôle in the guiding, checking and fixation of movement. The various symptoms of cerebellar disease which are grouped under the general heading of asynergia may be attributed to a disorder of this mechanism.

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