A CASE OF AMYOTROPHIC LATERAL SCLEROSIS WITH DEGENERATION OF THE MOTOR PATH FROM THE CORTEX TO THE PERIPHERY.

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THIS disease is considered by the French neurologists to be a distinct entity, but both Leyden and Gowers look upon it as a form of progressive muscular atrophy. It was first described by Charcot, who assumed that the primary lesion is degeneration of the pyramidal tracts, and that the affection of the grey matter is secondary or deuteropathic, even where the atrophy is atonic. This assumption is held to be unwarranted by Gowers[1] and Leyden, and the former states: "It is probable that the pyramidal tracts are degenerated, if not constantly, at any rate in such a very large proportion of the cases of progressive muscular atrophy, that Charcot's distinction is in effect giving a new name to an old disease." In the case which I am about to describe, the degenerative process seemed to have affected simultaneously and progressively the whole motor tract, viz.: cortex cerebri, pyramidal system, anterior horn cells, anterior roots, and the motor fibres, with corresponding spasmodic condition, and progressive atrophic changes in the muscles. I am led to believe this partly by the clinical phenomena, but more particularly by the condition of degeneration and sclerosis found in the motor tract. The following degenerations in

[1] "Diseases of the Nervous System," vol. i., "Spinal Cord and Nerves."

the brain have been described by various observers. *Kahler and Pick*[1] were the first to observe degenerations above the pons; they noted sclerosis in the external part of the middle third of the crus cerebri, and an atrophy of the central convolutions, as evidenced by the increased depth and breadth of the pre-central and central sulci. *Kowjewnikoff*,[2] of Moscow, described a case of amyotrophic lateral sclerosis, in which the degeneration of the fibres of the pyramidal system could be followed by means of granular bodies through to the cortex. In the peduncle, the sclerosis occupied the middle third of the crusta symmetrically on the two sides. Above, in the posterior part of the internal capsule, it was also found, and thence it was followed into the convolutions which border on the fissure of Rolando, being more marked in the ascending frontal than in the ascending parietal. He also noted a naked eye shrinking of the ascending frontal and of the lower part of the ascending parietal convolutions. *Charcot and P. Marie*[3] have confirmed the existence of these cortical lesions; they have noted also the disappearance of the large motor cells of the cortex, at the level of the para-central lobule and the intracerebral lesion of the centrum ovale, corresponding to the pyramidal bundle. In all these situations they have found granular bodies. *Lombroso*[4] has confirmed the existence of these granular bodies along the intracerebral tract of the pyramidal bundle. *Joffroy et Achard*[5] have described a case in which the central lesions were limited to the spinal cord and bulb with peripheral neuritis and muscular atrophy in the lower limbs.

Rovighi et Melotti[6] noted the integrity of the internal capsule and were only able to find degeneration starting from the peduncles.

[1] "Beitrage zur Pathologie und Pathologischen Anatomie des Central Nervens Systems," 1879, p. 157.
[2] *Centralblatt für Nervenheilkunde*, 1885.
[3] "Deux nouveaux cas de sclérose latérale amyotrophique," *Archive de Neurologie*, 1885, tome x., p. 1.
[4] *Lo Sperimentale*, 1888.
[5] *Archive de Médécine experimentale d'Anatomie et Pathologie*, vol. xi., p. 121, 1890.
[6] "Contributione allo Studio della Sclerose laterale Amiotrofica," *Revista sperimentale di Frenatria*, 1888, tome xiv., p. 315.

Paul Marie[1] has described a case of amyotrophic lateral sclerosis without any lesion of the pyramidal bundle at the level of the pyramids. Tooth[2] and Turner could not give any positive opinion, owing to decomposition of the internal capsule and crus cerebri, and this paper deals more with the origin of the cranial nerves.

In the spinal cord the sclerosis has been found limited to the tracts which are motor in function, viz., the crossed and direct pyramidal. The latter varies in size in different individuals, and therefore the sclerosis varies proportionally. Various observers have described a degeneration of the anterior ground bundle. Mœli, Leyden, Flechsig, Charcot and others, and Muratoff,[3] who quotes these authorities found that in all the cases where the anterior ground bundle is sclerosed, the posterior longitudinal bundle was also affected. This favours Flechsig's view that these two tracts are functionally analogous. A slight degeneration of the fillet has been observed in one case by Kronthal,[4] and in another by Muratoff.[5]

An important case has lately been described by Senator.[6] A woman who had all the symptoms of amyotrophic lateral sclerosis died. At the autopsy atrophy of anterior horn cells observed, but no sclerosis of lateral columns. There was renal atrophy and chronic vascular degeneration.

Tooth and Turner (*loc. cit.*) say: "It must be borne in mind that in many instances no change has been found in the peripheral nervous system." I am, however, of opinion that this statement is liable to fallacious interpretation. If the anterior horn cells are destroyed, the axis cylinder processes which form anterior roots and motor efferent fibres must perish; but it is possible that they leave no trace of their previous existence behind. With regard to the anterior horn cells, it is especially the anterior and internal groups that

[1] *Archive de Neurologie*, 1887, tome xiii., p. 337.
[2] "Study of a Case of Bulbar Paralysis with Notes of the origin of certain Cranial Nerves," BRAIN, part. lvi., 1891.
[3] Muratoff, *Neurol. Centralblatt*, 1891.
[4] Kronthal, *Neurolog. Centralblatt*, 1891.
[5] Muratoff, *Neurolog. Centralblatt*, 1891.
[6] *Wiener, Med. Wochenschrift*, Nov. 31, 1894.

are destroyed, the posterior and external to a less degree, and Clarke's column is usually not affected.

I will now give the clinical history, notes of autopsy and microscopical examination of my case, and I take the opportunity of expressing my indebtedness to Dr. Bruce for kindly allowing me to see the case in consultation with him, and also allowing me the use of the notes for publication.

Summary of Clinical Phenomena.—One year's duration. Commenced with weakness and numbness in right leg, gradually increasing, and attended with wasting of muscles and exaggerated deep reflexes followed by similar affection of right arm and hand, with especial wasting of thenar, hypothenar eminences and interossei. A little later left leg affected in a similar manner to the right, and then left arm and trunk. Terminated with bulbar symptoms, and probably paresis of diaphragm.

Sarah Albrow, age 39, dressmaker, admitted into Charing Cross Hospital, January 18, 1894. She had been seen on May 1, 1893, by Dr. Bruce, who made the following notes :—

Nervous debility in family. No previous illness of a serious nature, but for twelve months past her health had been failing. For the last five months she had been troubled with a feeling of cold in the right leg, from knee to toes, and a sense of weight in walking. The difficulty increased so that she dragged the right leg, which felt heavy and cold, and it commenced to waste. The right arm began to fail twenty-one days ago; gradually progressive weakness came on, just like the leg, but especially in the thumb and forefingers, and she experienced a difficulty in holding things. Exaggerated knee-jerks present on both sides, and ankle clonus especially marked on the right side. Sensation in no way affected. All the muscles of the upper limbs most irritable on tapping. Vision quite good. Hearing good. Visibly lame in right foot, shuffles it along, especially front part of it. Nothing definitely abnormal, pulmonary, or cardiac. Urine said to be normal. The patient was again seen by Dr. Bruce, and recommended to come into the hospital. The following notes were taken while she was in the hospital :—

Heredity.—Father and mother alive and healthy; brothers and sisters ditto.

Past Personal History.—Scarlet fever and measles when a child. From that time up to the commencement of present

illness patient was quite well. Up to the time of the present illness patient menstruated regularly.

Present Illness.—Commenced about ten months ago. Previous to this for about three months patient suffered with severe occipital neuralgia, and a feeling of languor and tiredness. This was followed by numbness, coldness and weakness in the *right leg*, so that she dragged it; then the *right arm* became affected in a similar manner. Later the *left leg* became affected, and finally the *left arm*.

For the last month she has been unable to stand or walk, owing to complete loss of power in the legs, and there has supervened a progressive weakness of the muscles of the back and neck, so that she is unable to hold her head up.

Present Condition. — Consciousness, comprehension, reason and memory good; no fits.

Spine.—Some tenderness in the cervical region.

Motion.—There is complete loss of power in the legs and arms. There is great wasting of the muscles of the upper and lower limbs and trunks, especially the small muscles of the hands, and the extensors of the forearm, the biceps and the deltoid, the small muscles of the feet, and the flexors of the knee and ankle. The intercostals and pectorals are also wasted.

There is a want of mobility of expression in the face, and this is more marked on the right side. Tongue is protruded in the mid line, and there is no fibrillary contraction. Her speech is somewhat slow, but there is no other impairment, and she is able to swallow perfectly well. Fibrillary contraction may be observed in the limbs and trunk. She lies on her back, with the arms adducted to the sides of the body. The forearm is semi-flexed in pronation; the wrist is flexed. There is marked wasting of the thenar and hypothenar eminences, and of the interossei, and the atrophy bears the Aran-Duchenne type. There is considerable rigidity in the shoulder, elbow and wrist, and movement causes pain. *Deep reflexes.* Elbow tap exaggerated on left side, and also on right, but much less marked.

Knee-jerk exaggerated on both sides.

There is a good deal of rigidity in the neck, and pain on movement.

The sphincters are unaffected, and all the special senses are perfect. There is no loss of sensibility to pain nor heat and cold.

Urine, no albumin, no sugar.

The wasting progressed daily until she became a living skeleton unable to move, and the breathing was mostly abdominal.

ELECTRICAL EXAMINATION.

A. Faradic Current.

Electric sensibility appears to be markedly increased.

Left leg.

The muscles of the leg do not react to a strong current.

To the very strongest current the

Extensor brevis digitorum gives a sluggish and feeble contraction.

The *peroneus longus* and *brevis* give only a faint flicker to the very strongest current.

There is no reaction in the muscles of the calf in either leg to the strongest current.

Right leg.

None of the muscles react to a strong current.

To the strongest current the

Flexor longus digitorum contracts sluggishly but fairly forcibly, and

The *extensor brevis digitorum* gives a faint and sluggish contraction.

The *dorsal interossei* on both feet do not contract to the strongest current.

Left thigh.

The extensor muscles, and notably the *vasti* contract feebly to a moderate current.

The *sartorius* gives a sluggish and feeble contraction.

There is no evidence of contraction in the hamstrings or adductor muscles, even to the strongest current.

Right thigh.

The *vastus internus and externus* react fairly to a moderate current, and slightly more than on the left side.

The flexor muscles and adductors do not contract.

The application of the pole upon the extensor muscles of both thighs causes marked patellar clonus.

Left arm.

The *brachialis anticus* and *biceps* respond to a strong current.

To the same current the *triceps* only gives a faint flicker, as also the *palmaris longus.*

Forearm.

Flexor profundus digitorum contracts sluggishly and feebly.

Flexor sublimis digitorum contracts sluggishly and feebly.

Flexor longus pollicis contracts well by comparison.

There is no contraction of any of the extensor muscles of the forearm.

Hand.

The dorsal interossei do not react to the strongest current.

The *abductor minimi digiti* gives a faint flicker, and the *flexor brevis pollicis* (the internal head) gives a forcible but very sluggish contraction.

Right arm.

To strongest current

Biceps and brachialis anticus, reaction nil.

Triceps, no reaction.

Forearm.

Flexor profundus and sublimis give faint and sluggish contraction, with a strong current, as also the *flexor carpi ulnaris.*

No reaction in the flexor longus pollicis.

Hand.

The flexor brevis pollicis contracts forcibly but sluggishly.

None of the other muscles of the hand react even to the very strongest current.

B. GALVANIC CURRENT.

Left leg and thigh.

Gastrocnemius and soleus contraction very weak. ACC > KCC.

Tibialis anticus. ACC > KCC.

Peronei. ACC > KCC.

No response whatever in extensor communis digitorum.

Extensor brevis digitorum normal.

Extensor muscles of thighs normal.

No response whatever in the hamstrings.

Right leg and thigh.

No contractions whatever in *gastroc. and soleus.*

Flexor longus hallucis. ACC > KCC.

Tibialis anticus. ACC > KCC.

Extensor brevis digitorum, no reaction, remaining muscles of leg normal, but very weak contraction.

Vastus internus, externus, and the rectus, contract normally and fairly strongly.

No reaction whatever in the hamstring muscles.

Left arm.

Biceps and brachialis anticus normal, but weak contraction.

Triceps no reaction.

Forearm.

Flexor profundus digitorum. ACC > KCC.

Flexor carpi ulnaris, normal, but very weak; no reaction in the extensor muscles.

No response in muscles of hand.

Right arm.

Biceps and brachialis anticus, normal, but very weak, no reaction whatever in triceps.

Forearm.

Flexor carpi ulnaris. ACC > KCC.

Flexor profundus digitorum. ACC. > KCC.

No reaction in the extensor muscles.

No reaction in any of the muscles of the hand.

Summary of Electrical Examination.

Extensor muscles of the thigh preserve for the most part their electric excitability.

The *extensor muscles* of the leg are electrically stronger than the flexors.

In the arms the flexor muscles are the stronger; the only muscles in the forearm which react at all well are the *flexor carpi ulnaris*, and the *flexor profundus digitorum*.

The muscles of the hands and feet appear to have lost almost entirely electric sensibility to both currents.

It was thought by the house physician, after she had been in the hospital a fortnight or three weeks, that there was some improvement in the movement of the legs; doubtless it was due to some of the spasmodic rigidity having become less.

She was troubled with pains in the limbs, waking her up from her sleep, otherwise she seemed no worse in her general health.

March 19.—At 10 p.m., patient had a new development of symptoms beginning with a sudden fit of coughing, followed by shortness of breath, and inability to sleep owing to the repeated attacks of coughing. When she was examined it was found that there was considerable dyspnœa and cyanosis of lips, the respirations 48, short and jerky. The diaphragm was overacting, and there was hardly any intercostal movement. In the lower part of the chest the interspaces were retracted with each inspiration. The right sterno-mastoid was not acting so well as the left. Pulse 108. Temperature normal.

Very little air is entering the left lung. Patient complains of a dull aching pain between the shoulders and in the legs. Oxygen was administered with an inhaler, but without much relief. Injection of morphia and strychnia ♏ 1½ of each was administered with benefit.

March 20.—The difficulty in breathing is diminished and she is less cyanosed. The left side of the chest hardly expands at all, the lower intercostal spaces are retracted, and the diaphragm is doing all the work.

March 21.—Respiration is quieter and less jerky, and appears to be carried on solely by the diaphragm. Patient's speech is rather indistinct, and she does not swallow so well.

March 22.—Respiration 30. Pulse 90. Her speech less distinct.

April 3.—Last night patient was suddenly seized with cough and a sense of oppression in breathing. The alæ nasi are working. Respiration 44. Marked cyanosis. Speech greatly affected, unable to swallow solid food, and nervous about taking liquids. Saliva dribbles from the angle of the mouth. No air entering left lung. The left side of chest does not move. Temperature 101·4°. Strychnia and morphia injections repeated. Her condition became worse and worse, and she died on April 4.

Autopsy.—Twenty-one hours after death by Dr. Arkle, who made the following notes:—

The body is greatly emaciated, rigor mortis well marked. Weather temperate. The body lies on the heels, buttocks and shoulders, owing to the arching of the back. Slight *post-mortem* staining of dependent parts of body. The hands are smooth and glossy, and the fingers are over extended and cannot be flexed. There is a marked wasting of all the small muscles of the hand and forearm, the thenar and hypothenar eminences. Toes of both feet flexed and ankle joints of both feet extended. Skin of feet smooth and shining. There is a very small abrasion the size of a lentil over the sacral region. On opening the chest, the following points were noticed: The lungs are very soft, congested, and there are caseous foci at both apices. Heart 7 oz., very small, otherwise normal to the naked eye. Abdomen—liver 40½ oz. normal, spleen 2½ oz., very small and pale. Kidneys weigh together, 7½ oz., small, red in colour, capsule very adherent.

Central Nervous System.—On removal of calvarium a good deal of blood escaped, the dura mater appears somewhat thickened. The longitudinal sinus contains a little fluid blood. There is an opacity and thickening of the arachnoid and pia mater, especially about the central convolutions. The Pacchionian bodies are unusually large. There is no thrombosis or blocking of the large vessels, nor any evidence of softening or growth. On slicing the cerebrum a great deal of congestion and increased vascularity was observed both in the grey and white substance, but no other naked eye hæmorrhage.

Spinal Cord.—On opening the spinal canal, an opacity and yellowish appearance of the arachnoid and pia mater presents itself, especially in the cervical and lumbo-sacral enlargements.

The Cord.—On cutting the cord it was noticed to be softer than natural in the dorsal region. The whole of the central nervous system and the following nerves, phrenics, vagus ulnar, median and sciatic nerves were placed in Müller's fluid for hardening.

After hardening the brain in Müller's fluid and transferring to spirit, I noticed that the ascending frontal and ascending parietal convolutions were shrunken below the level of the other convolutions, and the central and precentral sulci were deeper and broader than usual.

Microscopical Examination of the Central Nervous System.—After hardening in Müller's fluid, my methods of examination were as follows:—Pieces of tissue were stained by the Marchi method and embedded in celloidin. Other portions were placed in spirit and then embedded in celloidin, and sections of the same were cut and stained by Weigert-Pal carmine method and with hæmatoxylin and eosin.

Condition of Membranes and Vessels.—The pia mater is considerably thickened, in places laminated; the vessels are gorged with blood, and in their neighbourhood are enormous numbers of leucocytes. The neuroglia tissue is increased, and this is especially evident in sections of the cortex of the central convolutions just beneath the surface, the network of connective tissue being continuous with and extending from the pia mater. Sections of the brain and spinal cord stained with hæmatoxylin and eosin with a view to microscopical examination of the condition of the membranes and vessels exhibited the following points:—Thickening of the pia mater and marked congestion of the capillaries, small arteries and veins. The membranes covering the surface of the brain and dipping into the sulci exhibit a condition of chronic peri-arterial inflammation, being infiltrated with leucocytes, and in places laminated. The walls of the small vessels are thickened, and the muscular coat of the arterioles is somewhat hyaline in appearance. There are numerous small hæmorrhages. This condition of the membranes and vessels appears to be more manifest over the central convolutions than in the occipital lobes. The membranes and vessels of the spinal cord present a similar appearance, but not so marked. I regret that the kidneys were not preserved for examination. Their naked eye appearance and size suggested a chronic vascular degenerative change with overgrowth of connective tissue.

Brain and Internal Capsule.—Sections of the cortex of

the *central convolutions* showed numbers of granulation corpuscles, whereas sections of the occipital lobes showed none.

Sections of the cortex of the central convolutions stained by Marchi's method showed that numbers of nerve fibres had disappeared, also that numbers of fibres were undergoing degeneration. This was also manifest by the Weigert or Pal method, but the degenerating fibres cannot be seen nearly so definitely. *Vide* photo-micro., Plate III. (1). Sections of the occipital lobe showed no such degenerated fibres. Examination of a large number of sections revealed absence of the large pyramidal cells. The internal capsule showed a number of degenerated fibres stained black by Marchi fluid amidst empty spaces and sclerotic tissue. These degenerative appearances are seen in the posterior part of the internal capsule. *Vide* photo-micro., Plate III. (2), low power; the black dots are the degenerated fibres in cross section.

Crus Cerebri. — Sections were stained by all three methods with the same result, viz., sclerosis of the whole middle third, and amidst the sclerosed tissue black degenerated fibres can be seen by Marchi staining. *Vide* photo-micro., Plate III. (3), of a section of the crus cerebri stained by Weigert method. The middle portion is quite light, owing to its not being stained by the hæmatoxylin.

Pons.—The pyramidal fibres exhibit extreme degeneration and sclerosis. Fillet and superior cerebellar peduncles unchanged.

Medulla. — Pyramidal fibres, extreme sclerosis and degeneration. *Vide* photo-micro., Plate III. (4). Internal and external arciform fibres and interolivary layer normal. Slight sclerosis of posterior longitudinal bundle. Restiform body normal. Ventral cerebellar fibres degenerated (?). As these sections were only stained by Weigert method, I cannot say for certain whether this is so or not, but certainly the ventral cerebellar tract amidst the external arciform fibres does seem to have more neuroglia tissue than normal.

Nuclei of Grey Matter.—The only nuclei that seem to

be degenerated are the hypoglossal and the lower facial with which it is associated, and also the spinal accessory. Many of the cells have disappeared, and some are shrunken and pigmented.

Medulla, at the lower part of the decussation of the pyramids, stained by Marchi's method, showed a sclerosis, with numbers of black degenerated fibres just similar to the appearance presented in the cortex and internal capsule.

Cervical Spinal Cord showed atrophy of anterior horns, with disappearance of the anterior and internal groups of nerve cells, and to a less degree atrophy of the posterior and external groups. Sclerosis of the direct and crossed pyramidal tracts, and considerable atrophy of the ground fibres. The direct cerebellar tract, lying outside the crossed pyramidal tracts, is normal. *Vide* photo-micro. (5), Plate IV.

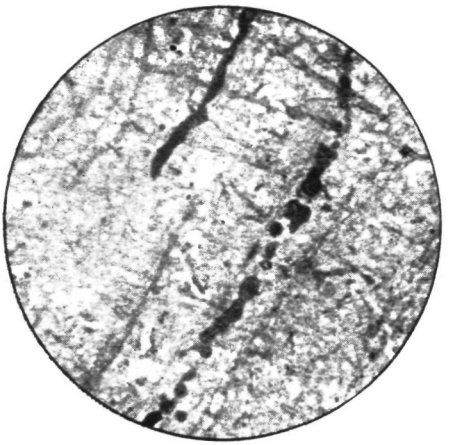
Dorsal Spinal Cord. — The anterior horn cells are atrophied. Clarke's column apparently unaffected. *Vide* photo-micro. (6), Plate IV.

Lumbo-sacral Spinal Cord and Roots.—Posterior roots normal. Anterior roots, great outfall of fibres. *Vide* photo-micro (10). Here again the anterior and internal groups of cells are most atrophied but the posterior and external group, although they have not disappeared, are undoubtedly undergoing degeneration. *Vide* photo-micro. (7), Plate IV., of this group of cells stained by Marchi's method. The cells are black, presumably from fatty degeneration (this is usually termed pigment, but it stains black with osmic acid). Many of them have their processes gone; some are shrunken, and some have swollen up.

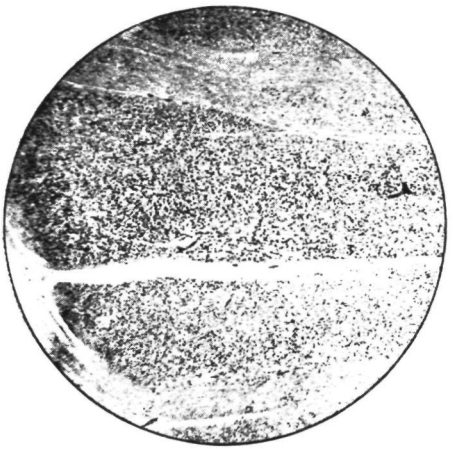
Nerves.—Phrenics stained with osmic acid and picro-carmine showed numbers of fibres undergoing degeneration. Vagus, treated in a similar manner, showed some fibres undergoing degeneration. Ulnar, median and sciatic showed very few fibres undergoing degeneration.

Sections of these nerves, however, stained by osmic acid and cut in celloidin, showed THAT A LARGE NUMBER OF FIBRES HAD BEEN DESTROYED, and many of the bundles were much smaller, so that a section of the ulnar, when

Plate III.



1.



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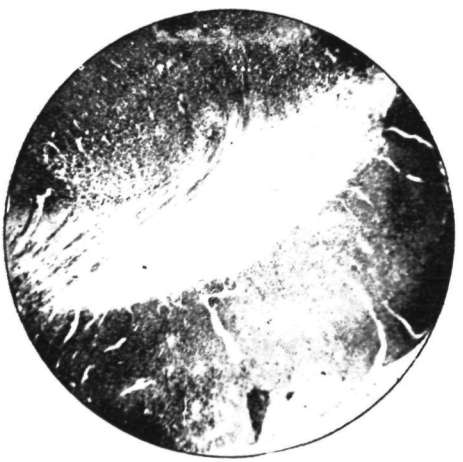

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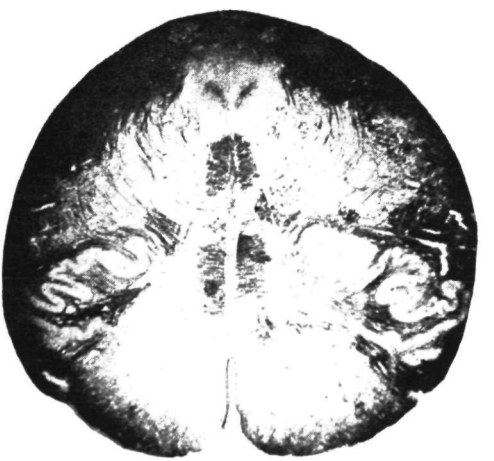

4.

Amyotrophic lateral sclerosis. (1) Degenerated fibres in cortex cerebri. (2) Transverse section of degenerated fibres in the anterior part of the posterior half of the internal capsule, both stained by Marchi's method. (3) Crus cerebri stained by Weigert's method, showing sclerosis of the middle third. (4) Medulla showing sclerosis of the pyramids also stained by Marchi's method. Photo-micrographs of untouched negatives.

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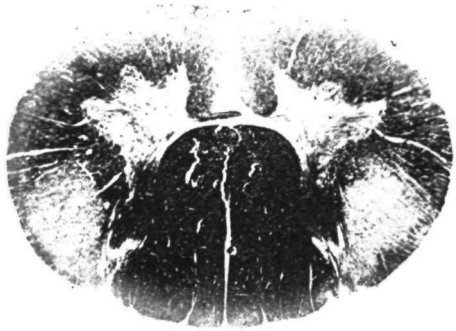
Plate IV.



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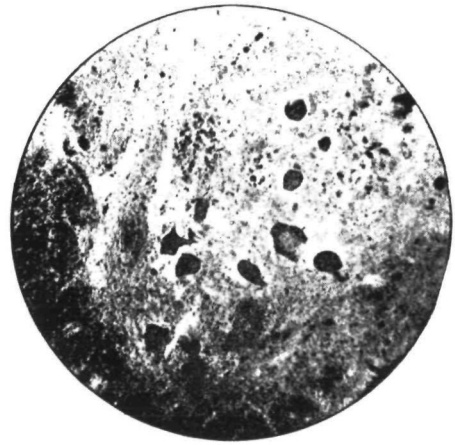

7.

Amyotrophic lateral sclerosis. (5) Spinal cord lower part of cervical enlargement. Sclerosis of pyramidal tracts and antero-lateral region. Direct cerebellar fibres seen unaffected outside crossed pyramidal tracts. (6) Spinal cord eighth, dorsal. (7) Posterior external group of cells of anterior horn in lower lumbar region, showing degenerative changes; the anterior internal groups have entirely disappeared in this section.

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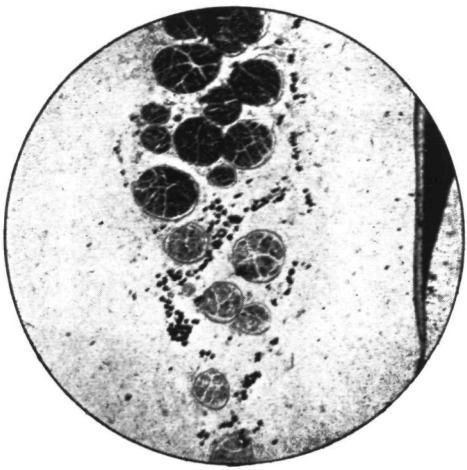
PLATE V.



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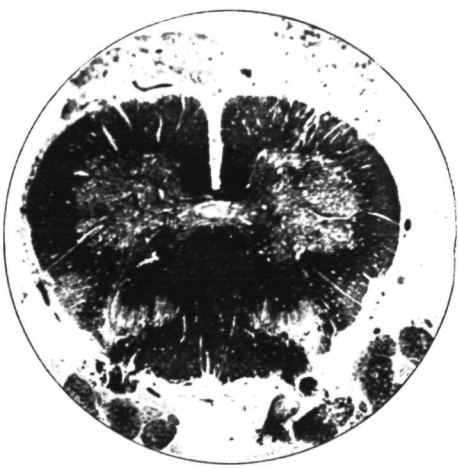

10.

(8) Ulnar nerve from the middle of the forearm, magnified about ten diameters, stained with osmic acid and cut in paraffin. The bundles in the upper portion are normal. The lower six bundles are greatly wasted and do not stain black. (9) One of these bundles highly magnified, shewing that a large number of fibres have completely atrophied. (10) Section of spinal cord in sacral region showing sclerosed crossed pyramidal tracts. Also compare colour of anterior and posterior roots, the former being degenerated.

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looked at with the naked eye, appeared much blacker and fuller in one half of the section than the other. *Vide* photo-micro., Plate V. (8) and (9). In fact, the section appeared to be divided into two parts, one in which the bundles of nerve fibres had shrunk to half their size, and another which was hardly affected at all. The photo-micro. (9) shows one of the sclerosed bundles of fibres. The sclerosis was less apparent in the median and sciatic nerves than in the ulnar. The appearance closely resembles the photo-micrograph of Dr. Sherrington's after section of ventral and dorsal roots, the latter cut proximal to the ganglion. Dr. Sherrington has, in a most valuable paper in the *Journal of Physiology*, October, 1894, shown that a nerve entering a muscle contains a large number of *afferent* muscular fibres. It would be interesting in any future case of amyotrophic sclerosis to examine a so-called purely motor nerve entering muscle to see if these afferent motor fibres are present. It may be that the half of the nerve undegenerated is purely sensory, while the other half so obviously atrophied is muscular, the undegenerated fibres being those afferent muscular fibres of Sherrington. This is very probable, as in the monkey I have found that the ulnar nerve can be split into two portions, one which by stimulation, either by faradism or ligature, is followed by muscular contraction, and another, presumably cutaneous, which gives no such result.

This case has many points of interest. I believe that a simultaneous degeneration of the upper and lower segments of the motor path took place, and the clinical history supports this opinion, for there was wasting of muscles appearing at the same time as exaggerated reflexes. The hemiplegic onset of first the right leg, then the right arm, and subsequently left leg, then left arm, supports the view held by Charcot that the disease is primarily in the upper segment; but against this we have the fact that there was muscular wasting of the typical progressive muscular atrophy type associated with the spasmodic conditions. Are we to believe that the degeneration of the upper segment of the motor path begins in the terminations of the crossed pyramidal tracts in the spinal cord and spreads gradually

upwards? Or is it due to degenerative changes in the cortex[1] leading to degeneration and atrophy of the large cells of the third layer which give origin by their axis cylinder processes to the fibres of the pyramidal tract? There is nothing against the latter view in this case, at any rate, although cases in which no degeneration can be found above the pons would support the former view. My own experience of experimental degenerations of the cross pyramidal tracts in monkeys produced by various injuries of the cortex, ablation, subcortical section, and cauterization, lead me to believe that if the connection of the neuron with its cell be destroyed, a degeneration occurs throughout the whole pyramidal system, and does not creep down nor creep up the fibres forming it. It may, however, be different in the case of a slow degenerative process affecting the protoplasmic processes of the cells, which, as Golgi and Ramon y Cajal have shown, bear a most complex arrangement, *like a tree*, and we can easily understand how a chronic peri-arteritis could interfere with the nutrition of the cell, specially as we are led to believe that these dendritic processes project into corresponding lymph spaces which are in connection with peri-vascular lymphatics. Interference by chronic inflammatory changes, such as are found in this case, might very well cause nutritional changes in the cell, eventually leading to its complete atrophy and disappearance. As a rule, the more remote a part is from its seat of nutrition, the more likely is it to undergo degeneration, and we could thus explain the gradual "creeping up" of the degenerative process.

Certainly the appearances of degeneration and sclerosis presented by the internal capsule and the crus cerebri in this case were quite as advanced as the pyramidal tracts of the medulla and dorsal region of the cord.

Of course in the white matter of the hemispheres of the centrum ovale, the process of degeneration could only be seen by scattered degenerated motor fibres and granulation cor-

[1] This view is supported by the cases of Kahler and Pick, Kowjewnikoff Lombroso, and Charcot and Marie.

puscles, and owing to the large number of intermingled healthy fibres not belonging to the pyramidal system, it is difficult to recognise sclerosis, although when portions of the cortex of the motor area are stained by the Weigert method and compared with the occipital region, there is a marked difference in the appearance of the fibres of the sections of these two areas. By Marchi's method, however, degenerated fibres, such as shown in the photo-micrograph, could be found throughout the sections of the motor area (especially numerous in parts where the disease was not so advanced as in the lower part of the Rolandic area), but none in sections of the occipital, a purely sensory area. Where the pyramidal tract occupies a small area, as from the internal capsule downwards, the degeneration after staining the sections, is apparent to the naked eye.

It is difficult to understand why, in the spinal cord, the anterior horns alone should suffer, and why particular groups in particular regions—such as the cervical and lumbar enlargements, and the *anterior and internal groups of cells*—be completely destroyed, *while the posterior and external escape;*[1] why the posterior vesicular column, and the direct cerebellar tract which arises from it should be unaffected, if this disease depended solely upon a chronic inflammatory process. If, however, we look upon this progressive muscular atrophy as a degenerative process of the motor path, affecting in some cases the lower segment first, therefore masking the symptoms which would be produced by the subsequent affection of the upper segment, or, in some cases, in the upper segment first, producing characteristic symptoms, or affecting as in this case both segments of the motor path simultaneously; we must then conclude that there is

[1] Is it possible that the escape of the extensor muscles of the thigh and leg may be associated with the preservation of the posterior and external groups of large multipolar cells in the lumbo-sacral region? The preservation of these cells and the disappearance of the cells of the opposing ham-string muscles which were found to have lost all electrical excitability (and presumably, therefore, innervated by cells of the anterior internal groups which had disappeared) would account for the exaggeration of the knee-jerk which was noticed, even within a month or two of the patient's death. This fact might also serve to account for the exaggerated tendon reflexes observed in Senator's case where the *post-mortem* examination revealed no sclerosis of the pyramidal tracts.

wanting in the cells, and their processes which constitute the motor tracts, that due and necessary power of adapting repair to waste even under unfavourable nutritional conditions, such as might be produced by a general chronic vascular change, hence their degeneration.

If it were hereditary, as Friedreich's disease, we could assume it was a general defect in the "*make up*" of the cells and fibres of the motor side of the nervous system rather than an acquired condition, but in only a few cases has an hereditary history been obtained.