Study of a case of bulbar paralysis, with notes on the origin of certain cranial nerves. By Howard H. Tooth MD FRCP and William Aldren Turner MB MRCP. Brain 1891: 14; 473–495; and A case of amyotrophic lateral sclerosis with degeneration of the motor path from the cortex to the periphery. By Frederick W. Mott MD FRCP, Assistant Physician, Charing Cross Hospital. Brain 1895: 18; 21–36.

Under the general heading of chronic spinal muscular atrophy, (Sir) William Gowers ([1845–1915]: A Manual of Diseases of the Nervous System; Volume 1: 1886, pp. 356–381) grouped progressive muscular atrophy, wasting palsy, amyotrophic lateral sclerosis and chronic polio-myelitis: ‘the diseases are characterized by slow wasting of the muscles, spreading and increasing until it is wide in extent and extreme in degree, and dependent on slow degeneration in the ganglion cells of the anterior column of the spinal cord and of the pyramidal tracts’. Known to (Sir) Charles Bell (1774–1842) and Jean Cruveilhier (1791–1874), and named by François Aran (1817–61) who considered the disorder to be primarily of muscles, Jacob Augustus Lockhart Clarke (1817–80) first attributed these disorders to damage of grey substance in the spinal cord; and Jean-Martin Charcot (1825–93) associated the atrophy with wasting of the ganglion cells. Gowers recognized that the conditions are not confined to the spinal cord—the nerve cells from which the motor bulbar nerves arise often also being affected, making progressive bulbar paralysis another member of this group of wasting disorders. Acknowledging the existence of two forms, Charcot restricted the use of amyotrophic lateral sclerosis to the ‘deuteropathic form in which the pyramidal tracts and cornua are involved’, retaining the term ‘progressive muscular atrophy’ for cases with muscle wasting only.

Revising the account for volume one of his third edition (1899, pp. 531–558: all that was published), Gowers was able to draw on work emphasizing that the seat of the disease is confined to motor tracts—crossed and direct pyramidal, anterior ground bundle and posterior longitudinal fasciculus—and mainly in the cervical cord. The main microscopic feature is disappearance of nerve cells within the central grey matter. With involvement of the brainstem, the hypoglossal nucleus is targeted but the oculo-motor nuclei spared. Peripheral nerves, either of the cranium or extremities, may be involved. Everything suggests that the changes are degenerative and not due to focal disease such as myelitis. Whether they begin in the parenchyma or interstitial tissue is difficult to assess since both lead to diffuse sclerosis; and pathological examination early in the course of the disease is rarely possible. What remains less clear is the status of chronic progressive bulbar paralysis. Dr (John) Hughlings Jackson (1835–1911) has granted Tooth and Aldren Turner permission to report a case in which ‘a primary affection of cells and fibres, motor in function, seems the only explanation which our present knowledge can justify’.

In December 1887, G.W.V. (aged 48 years) began to lose his voice and, soon after, noticed stiffness and weakness of the right arm and leg. Within a few months, he had difficulty with breathing and could not cough. By October 1888, G.W.V. is emaciated, displaying the attitude of ‘sad inanimate expression with the temperament buoyant and expectant’ that characterizes this disease. The facial muscles are weak; the tongue is immobile and speech confined to a quiet inarticulate noise. Comprehension is intact as are the special senses and function of the sphincters. G.W.V. laughs and sobs inappropriately. Communication is by writing. Dr (Sir Felix) Semon (1849–1921) has examined his throat and palate and laryngeal paralyses. There is wasting and weakness of the right hand. The tendon reflexes are brisk, the voice and, soon after, noticed stiffness and weakness of the right arm and leg. Within a few months, he had difficulty with breathing and could not cough. By October 1888, G.W.V. is emaciated, displaying the attitude of ‘sad inanimate expression with the temperament buoyant and expectant’ that characterizes this disease. The facial muscles are weak; the tongue is immobile and speech confined to a quiet inarticulate noise. Comprehension is intact as are the special senses and function of the sphincters. G.W.V. laughs and sobs inappropriately. Communication is by writing. Dr (Sir Felix) Semon (1849–1921) has examined his throat and palate and laryngeal paralyses. There is wasting and weakness of the right hand. The tendon reflexes are brisk, the gait hemiplegic. Over time in hospital, the wasting progresses and weakness extends to all four limbs. Eating becomes impossible and head control is lost. Agonal examination confirms wasting and weakness of the bulbar and limb muscles, sparing the eyes and with sensation intact. Post-mortem examination (Fig. 1) is carried out soon after his death (exitus lethalis) on 1 April 1889.

Microscopic examination of the upper brainstem reveals no loss of nerve cells in the third nucleus. The posterior longitudinal...
bundle is intact but the pyramidal tracts are degenerated. Lower sections have been mislaid so the next level to be examined is through the trigeminal nucleus. This shows severe nerve cell loss in the motor part but without involvement of the sensory elements. Both descending pyramidal tracts are severely degenerated with few remaining intact fibres of any size at this level and below. The 6th, 8th, 9th (including the nucleus ambiguus), 10th and 11th nerves are intact but the 7th nucleus is severely degenerated and the facial nerve much reduced in size throughout its intra-parenchymal course. The hypoglossal nucleus receives special anatomical attention. Based on their studies of normal individuals, the authors expect around 20–40 ganglion cells to be visible in each section. Proceeding from the relatively preserved rostral part, they find neuronal density reduced to four or five ganglion cells as increasingly caudal sections are examined until the nucleus becomes entirely atrophic. By contrast, the ‘small-celled nucleus of the hypoglossal’ is intact as are all other structures including the cerebellar and olivary nuclei. In the spinal cord, the gracile and cuneate tracts are normal but the anterior horns are devoid of nerve cells. The crossed and direct pyramidal tracts can be discerned but they are both much affected to the level of cervical iv (C4). At each descending level, the same appearance is apparent: atrophied anterior horn cells with extensive involvement of the pyramidal tract, which appears sclerotic, although still containing a few healthy looking fibres. The emerging fibres are thin but give rise to surprisingly healthy looking anterior nerve roots. The pathological changes are much less marked, although still present, towards the lower end of the spinal cord. It seems that this is a disease of the pyramidal tracts in the pons with descending degeneration: ‘the ganglion cells of the anterior horns...are deeply degenerated, yet the anterior roots are perfectly healthy...[although] the hypoglossal and facial nerves are much thinned by the disappearance of many nerve fibres...we can offer no explanation of this apparent anomaly’. Tooth and Aldren Turner consider that their anatomical and clinical observations indicate a contribution to innervation of the orbicularis oculi muscle conveyed within the facial nerve but originating from the oculo-motor and hypoglossal nuclei; and, by the same analysis ‘the eleventh nerve...is known to contain motor fibres for the palate and vocal cords...its nerve roots may be regarded as the lowest fibres of the vagus and its nucleus as the lowest part of the vagus nucleus...motor fibres which innervate the palate and larynx are...[also] derived from...the region of the hypoglossal nucleus’.

(Sir) Frederick Mott (1853–1926) sets out the contrasting views of Charcot and Gowers on the (deuteropathic) nature of amyotrophic lateral sclerosis and progressive muscular atrophy.
Figure 2  Amyotrophic lateral sclerosis. (A) Degenerated fibres in cortex cerebri. (B) Transverse section of degenerated fibres in the anterior part of the posterior half of the internal capsule. (C) Crus cerebri showing sclerosis of the middle third. (D) Medulla showing sclerosis of the pyramids. (E) Spinal cord lower part of cervical enlargement. Sclerosis of pyramidal tracts and antero-lateral region. Direct cerebellar fibres seen unaffected outside the crossed pyramidal tracts. (F) Posterior external group of cells of anterior horn in lower lumbar region, showing degenerative changes; the anterior internal groups have entirely disappeared. (G) Ulnar nerve from middle of the forearm. The bundles in the upper portion are normal. The lower six bundles are greatly wasted.
with Gowers concluding that ‘Charcot’s distinction is in effect giving a new name to an old disease’. Mott’s review of the literature seems familiar. It is unforgivably reminiscent of that written by Tooth and Aldren Turner and, in commenting on their work, has the added barb that ‘I am however of the opinion that [the] statement that...[no change is found in the peripheral nervous system]...is liable to fallacious interpretation...[since]...if the anterior horn cells are destroyed...the anterior roots and motor efferent nerves must perish’. Mott’s case, showing that the disease affects simultaneously the entire motor system from cortex to anterior horn cell with consequential spasticity and atrophy of the dependent muscles, is reported courtesy of Dr (John Mitchell) Bruce (1846–1929).

Sarah Albrow, a dressmaker aged 39 years, presents in May 1893 with wasting and weakness initially of the right leg but spreading to all four limbs and her neck muscles over a few months. Examination confirms facial weakness; wasting, weakness and extensive fibrillar contractions of the limbs; brisk tendon reflexes; but intact sensation, special senses and sphincter control. Thereafter, ‘the wasting progressed daily until she became a living skeleton unable to move, and the breathing was mostly abdominal’. Detailed electrical examination by Faradic and Galvanic currents is carried out. In hospital, Sarah has fits of coughing and despite rallying for a while with supportive measures, she is distressed and, unable to swallow, dies on 4 April 1894 after being given strychnia and morphine for symptomatic relief, ~15 months after the onset. The autopsy is performed by Dr (Charles Joseph) Arkle (1861–99: capped for England at Rugby football in 1886). Macroscopically, the frontal and parietal convolutions are shrunken. Microscopically, there is nerve cell loss, large pyramidal cells being entirely absent; and evidence of fibres undergoing degeneration in the cortex of the central convolutions, but not the occipital lobe, and internal capsules where the few surviving elements are within empty space and sclerotic tissue (Fig. 2). This is also the appearance of motor pathways within the crura cerebri,pons and medulla. There is degeneration of the hypoglossal and lower facial nuclei and also the spinal accessory nucleus. Their cells are shrunken and pigmented or missing altogether. Throughout the cervical, dorsal and lumbar cord there is loss of anterior horn cells, sclerosis of the crossed and direct pyramidal tracts and atrophy of the ‘ground fibres’. Mott is at pains to emphasize that ‘A LARGE NUMBER OF FIBRES [in the peripheral nerves] HAD BEEN DESTROYED’ although some bundles are preserved. This finding suggests that these are afferent fibres derived from muscle spindles as recently described by Dr (Sir Charles) Sherrington (1857–1952); and Mott wishes that he had examined ‘so-called purely motor nerves’ and so distinguished the degenerate efferent from the (putative) intact afferent bundles. 

Dr Mott ‘believes 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’. What remains uncertain is whether the central component begins in the cortex and descends, or in the terminations of the pyramidal tracts in the cord from where it ascends. While the absence of any pathological change above the medulla in some cases supports the ascending doctrine, the fact that degeneration will invariably be most marked at the extremity of the dependent nerve fibres following injury of the cell body is consistent with the hypothesis that the disease process begins in the cortex. In the case that he reports, no such distinction is apparent since the entire motor pathway is clearly involved.

What is the nature of the condition? The patchy involvement of the cord must be explained: that ‘the cervical and lumbar enlargements and the anterior and initial groups of cells...are completely destroyed whereas the posterior and external escape; why the posterior vesicular column and the direct cerebellar tract which arises from it should be unaffected’ makes it unlikely that amyotrophic lateral sclerosis is due to a local disease process such as inflammation. Rather ‘there is wasting 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...if it were hereditary...we could assume that it was a general defect in the “make-up” of the cells and fibres...but in only a few cases has an hereditary history been obtained’. More than one hundred years later, the aetiology and pathogenesis of amyotrophic lateral sclerosis remain largely unsolved; and the pathological substrate has undergone revision and extension as the spectrum of neurodegenerative diseases with wasting has evolved. The accelerated clinical course to death of G.W.V. and Sarah Albrow over only a few months in 1889 and 1894, respectively, reminds us of the poignant nature of this most awful of neurological diseases in which a seminal and hitherto poorly recognized contribution was made by Lockhart Clarke, as Martin Turner and colleagues point out in their occasional paper (page 3470).

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