HANDBOOK OF CLINICAL NEUROLOGY

VOLUME 22

SYSTEM DISORDERS AND ATROPHIES

PART II

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Edited by

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in collaboration with

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Foreword to volumes 21 and 22

Quite a number of neurological function disorders have benefited from the considerable advances which have been made since the turn of this century (for example, the discovery of slow-virus disease, dopamine deficiency in parkinsonism and GAD deficiency in Huntington's chorea, immunopathological mechanisms, dexamethasone's protection in serious central craniocerebraltrauma, and the value of vascular surgery in occlusive cerebrovascular disease). The application of advanced biomedical methods, procedures and apparatus have necessitated a more simple rearrangement of nervous and muscular disorders along lines which essentially represent cause and pathogenesis, rather than phenomenology. Neurological nosology has, in general, become somewhat more simplified.

One fairly large group of disorders has been left behind, however, in this elucidatory process and yet it belongs more or less to the very heart of clinical neurology, i.e. the heredo-'degenerative' disorders. The term degenerative arouses no small amount of opposition amongst a number of our colleagues, due to the supposed pejorative element attaching to it. The Editors are not able to share this view. Their own thoughts on the subject are given in the Forword to Volume 13 and remain unaltered.

Spinocerebellar degenerations, pyramidal tract degeneration, 'system' degenerations and such like constitute a large field of disorders, the study of which, in the Editors' view, has not progressed much beyond the descriptive level. In general, this is probably due to the fact that it is much less difficult to elucidate the pathogenesis of disorders in which some intermediate metabolite appears as a pathological storage product, than to discover why a part of the nervous system disintegrates without leaving remnants testifying to the nature of the disease process. As a consequence, the treatment of these disorders is alleviatory and palliative rather than rational and effective. Perhaps only a neurologist can experience those particulier feelings of inadequacy which manifest themselves when one is called upon to assume the care of a patient with amyotrophic lateral sclerosis, or progressive spinal muscular atrophy, Strümpell-Lorrain's disease, bulbar paralysis, or olivopontocerebellar degeneration. These volumes embody the current state of our knowledge on these disorders. Neurology has still to find the answers to these disorders and their victims must continue perforce to suffer. The Editors hope, however, that these volumes will contribute

not only to a greater understanding of them, but, hopefully, also to fresh attempts to solve their encumbering riddles.

The main ordinate of lay-out is topographic: firstly, those disorders involving the nerves, followed by those involving the spinal cord, and concluding with those of the cerebellum and brain stem. The Editors have maintained the attitude of reluctant splitters. In their opinion, the moment of lumping together has not yet arrived. Since the knowledge necessary to decide in this matter is not available, they have not forced their view on the authors.

These volumes, originally planned in 1967, have had to sustain a large number of delays, not the least of which were manuscripts lost in transit, authors who proved more than difficult to reach, and so on and so on. A great blow was dealt by the lamented death of Professor Lumsden, who was to have written a major introductory chapter. In him, neurology has lost an internationally acknowledged expert.

Although it is perhaps inviduous to single out particular authors for special mention, the Editors must use this occasion to confirm their indebtedness to their colleagues Eadie, Sutherland, Tyrer, Zeman, Norris and Dubowitz. To them and our other colleagues, the Editors owe their sincere thanks for the excellence of the contents of these volumes.

In a somewhat unusual departure from custom, the Editors are happy to acknowledge the debt they owe to the three desk editors concerned with these volumes, Mrs. L. Philipp, Mrs. W. H. Posthuma, and Mr. R. W. Stanley, for having helped us with their production. Their sense of purpose was of great encouragement in our labours.

Having concluded our paean, we must leave it to the reader to determine whether we are right in believing that these two volumes provide that level of coverage needed for a group of syndromes essentially constituting the main challenge to current clinical neurology.

P. J. V.
G. W. B.
J. M. B. V. de J.

Acknowledgement

Several illustrations and diagrams in this volume have been obtained from other publications. Some of the original figures have been slightly modified. In all cases reference is made to the original publications in the figure caption. The full sources can be found in the reference lists at the end of each chapter. The permission for the reproduction of this material is gratefully acknowledged.

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Contents

CHAPTER 1

Adult spinal motor neuron disease

Progressive muscular atrophy (Aran's disease) in relation to amyotrophic lateral sclerosis

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A disease seen rarely in adults is characterised by slowly progressive muscular weakness accompanied by wasting proportionate to the weakness in the affected muscles. There are occasional involuntary, fascicular twitches and painful muscle cramps in both the weak and normal muscles. The early symptoms tend to be in the arms and hands but in some cases the onset is in other limb muscle groups. Wherever it is first manifest, the weakness tends to spread during the subsequent months or years to the other muscles of both arms and legs and also the trunk and neck. The respiratory muscles are usually (but not always) the least affected until late in the course; the bulbar muscles also tend to be spared early and involved late.[1]

Examination reveals flaccid weakness; the muscle stretch reflexes are absent or, with early involvement, present but hypoactive. The stretch reflexes as well as the wasting and fasciculation are generally proportionate to the weakness, so that a patient unable to lift his arms or clench his fingers but able to walk and climb stairs will usually be areflexic in the arms but not the legs. The plantar responses, however, whether 1 limb is paralyzed or 4, show either flexion or no reaction (as when the flexor hallucis muscle is paralyzed). The mind is clear and the intellect is not affected; sensation is also normal and the control of bladder and bowel sphincters is preserved.

Most authors credit Aran and Duchenne with the priority in describing this disease, for which we continue to use the name suggested by Aran (1850), progressive muscular atrophy. To the experienced clinician, the clinical picture in adult progressive muscular atrophy is usually a stage in amyotrophic lateral sclerosis, and the difference between amyotrophic lateral sclerosis and progressive muscular atrophy will be a major theme of this chapter. In brief, the usual points of difference are as follows.

Progressive muscular atrophy tends to develop in the third to fifth decades, whereas the mean age of onset in amyotrophic lateral sclerosis is in the sixth decade (Table 1) or possibly even higher (Kurland et al. 1969). Progressive muscular atrophy has greater predilection for males than amyotrophic lateral sclerosis (Müller 1952; Table 1). Progressive muscular atrophy usually involves the bulbar muscles mildly and late in the course, if at all. Amyotrophic lateral sclerosis sometimes commences with bulbar involvement and usually causes some degree of pseudobulbar palsy. Progressive muscular atrophy reduces or abolishes the stretch reflexes, amyotrophic lateral sclerosis usually results in hyperreflexia, sometimes to a very marked degree including sustained clonus precipitated by such minor stimuli as normal

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postural adjustments or attempts to use the muscles. The rule of flaccidity in progressive muscular atrophy contrasts with the frequency of spasticity in amyotrophic lateral sclerosis. Fasciculation and cramps occur in both progressive muscular atrophy and amyotrophic lateral sclerosis but are more prominent in amyotrophic lateral sclerosis. Spontaneous and continuous, coarse, generalized fasciculation is rare in progressive muscular atrophy but common in amyotrophic lateral sclerosis (Swank and Putnam 1943). On the other hand, fascicular muscular contraction ('contraction fasciculation') usually seems more evident in the severely wasted muscles of progressive muscular atrophy patients. Plantar responses are always flexion or no reaction in progressive muscular atrophy, but range from flexion to extension in amyotrophic lateral sclerosis depending on the stage of that disease, eventually becoming extension in most cases.

The course in progressive muscular atrophy is usually very long, sometimes in excess of 20 years (Müller 1952), whereas half of the patients with amyotrophic lateral sclerosis are dead within 3 years and 90% within 6 years (Mulder and Espinosa 1969).

The gross pathology is usually normal in both progressive muscular atrophy and amyotrophic lateral sclerosis except for motor root atrophy. The microscopic examination reveals mainly lower motor neuron degeneration in the brain stem and spinal cord in progressive muscular atrophy; in amyotrophic lateral sclerosis these lesions are accompanied by demyelination of the corticospinal tracts and a lesser degree of neuronal disease in the cerebral motor cortex.

Experienced observers of the motor neuron diseases will recognize exceptions to these points of difference, but they serve to outline the essential clinicopathologic picture of progressive muscular atrophy.

HISTORY

Although it has been fashionable to credit Duchenne equally with Aran, partly because Aran (1850) acknowledged learning some details of muscle testing from Duchenne, Aran was not without status at the time and the actual writings do not suggest a student relationship to Duchenne. After his student days at Hôtel Dieu, Aran passed a distinguished medical career in Paris. His first published paper was on lead colic (Aran 1840) but his lifelong interest in all medical problems was presaged 2 years later by a paper on lung abscess (Aran 1842a) and a handbook on heart disease (Aran 1842b).

In January, 1847, Aran had become physician to the Bureau des Hôpitaux and probably became the regular medical correspondent for the 'Clinical review' in the new journal l'Union médicale. An unsigned column appeared first on 9 January 1847 The medical column for 17 July (completed in the issue for 20 July) bore Aran's initials for the first time. The topics were albuminous nephritis and the medical applications of tonics. According to the journal's index for 1847, Aran is credited with all the medical reviews that year, and this is substantiated by the internal evidence from comparing the style of the signed and the unsigned columns: all were evidently written by the same hand. At any rate, 14 different columns initialed by Aran appeared in 19 issues in 1847.

His penchant for lengthy columns increased in 1848 when only 14 of the popular columns required space in 26 numbers on a wide range of topics (e.g. purulent ophthalmia, alopecia, pneumonia, aortic aneurysm). In one of these columns he described a new syndrome of partial atrophy of the limbs which appeared in the 'Clinical review' for 25 November 1848, and was later also published in Aran's (1850) paper. This case report is summarized below in the section on progressive muscular atrophy as Case 2.

The remainder of this article, in l'Union médicale for 28 November 1848, discusses possible etiologies and then goes on to other topics: albuminous nephritis and whether heart disease, particularly that associated with cardiac hypertrophy, can lead to apoplexy. According to his report in 1850, Aran's attention was drawn to the patient described in Case

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2 by Rayer, then Chief of Service at 'la Charité'. Significantly, it was also Rayer who influenced Charcot toward study of diseases of the nervous system (Guillain 1955).

By the time of the second and more well-known report, Aran (1850) had been able to review the literature more carefully and no longer believed that the syndrome was unreported until 1848. He credited Sir Charles Bell (1830) with mention of 2 possible cases, and Darwall (1831) with 2 more, including possible benefit from the therapeutic use of electricity. Graves was cited for the case of an officer who developed amyotrophy of the arms in 1795 when 60 years old, but progression ceased in 1800 after mercurial treatments. Aran (1850) also cited cases described in older children by Abercrombie and Dubois, which are discussed below. Under the title 'atrophie musculaire progressive', Aran then described 10 patients seen since 1848 by himself and Duchenne, who attempted galvanotherapy.

In the meantime, we can trace Aran's career through 1860 and speculate why this brilliant physician has fallen into obscurity. One reason probably stems from Aran's lifelong concern for all medical problems, not just those of neurology, so that he excluded himself from the exciting neurological controversies soon to develop. His book on heart disease has been mentioned (Aran 1842b); another book dealt with diseases of the uterus (Aran 1858–60). Poor health was also a problem; his l'Union médicale column was suspended on 22 February 1849 because of illness. The series was never resumed; his next contribution was as an editorialist, commencing with a leading article on opium smoking in the number for 19 October 1850. Meantime, the famous article on progressive muscular atrophy was published and this must have been a major activity during his convalescence. Subsequent leading articles dealt with his usual broad range of interests including the public lavatories, discussed in the number for 17 December 1850.

Aran's review of the account by Meryon (1852) of sex-linked hypertrophic muscular dystrophy is particularly poignant since the recognition of that disorder has also been credited to Duchenne. With startling prescience, Aran wrote, in reference to Meryon's pathological (including microscopic) studies, that the end-stage of muscular degeneration might be the same in quite different diseases (Aran 1853).

By 1858 Aran had been elevated in the Paris faculty to 'Professeur Agrégé' at the Hôpital St. Antoine. Although this position saw ever new interests develop (e.g. Aran 1858–60), he continued an active interest in progressive muscular atrophy and contributed 2 of the 3 necropsies for one of Duchenne's (1859) later papers. Unfortunately, no likeness of Aran and few other details of his life were found during searches of public, hospital and university archives in Paris.

PROGRESSIVE MUSCULAR ATROPHY

The following case histories were published by Aran in 1850.

Case 1. A farm boy noted the onset of progressive arm and shoulder girdle muscle weakness with marked wasting at the age of 16 years. The forearm muscles also became involved but only to a mild degree. Joint and neuralgic pains occurred in the second year of the illness. A variety of treatments seemed to give only slight improvement and were abandoned because a cure seemed hopeless.

This patient was probably not seen by either Aran or Duchenne; Aran found the case reported by Dubois (1847). The age of onset, the rapidity of the wasting, and the pain make it difficult to identify the illness; polymyositis?

Case 2. Bernard, a man 47 years old, had always done vigorous work with his arms and hands. He was reported to have contracted syphilis in the past without known sequelae. He first noted progressive hand weakness in August, 1847. At the same time, his legs became less strong from day to day. He was nevertheless able to continue his employment until January, 1848. The examiners were struck by the patient's general appearance of good health in the face of the terrible disease to be described. There was marked forearm and hand muscle weakness and wasting. The arm and shoulder muscles were thought to be normal as were all the leg muscles (despite the patient's complaint). A physician doing research on the application of electricity to the

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treatment of diseases of the nervous system, M. Duchenne' evoked galvanic responses in the forearm muscles but most of the hand muscles were inexcitable. The electricity was perceived normally. Sulfur baths gave no benefit (Aran 1848). To this was added in 1850 a report of Duchenne's own examination of the patient to substantiate Aran's observation, and a follow-up note: painful cramps in the upper limbs diminished as the atrophy advanced, and occurred later in the legs along with almost lancinating pains.

Despite the credit given above to Rayer and Aran for appreciating the new syndrome seen in this case, the history of syphilis and the subsequent appearance of lancinating pain would today raise serious question of spinal meningovascular lues with amyotrophy (see below and Martin 1925) rather than progressive muscular atrophy.

Case 3. A stonemason noted the onset of weakness in the right arm at the age of 38 and was studied at 'la Charité' 2 years later. Strength was lost little by little and then he noted weakness which also progressed gradually in the left arm. Examination revealed marked involvement of the arm and shoulder girdle muscles, and also of the dorsal paraspinal muscles. The arm muscles were less wasted than the shoulder muscles, and the forearm and hand muscles less involved. Duchenne carried out galvanic testing and demonstrated contraction which was reduced in proportion to the muscle wasting. The severely affected deltoid muscle, for example, produced only feeble 'fibrillary' contractions in response to the stimulation. The patient called to their attention that he obtained some use of these muscles on arising in the morning but toward evening, or when fatigued earlier, found it impossible to use them. The original interview did not include questioning about muscle twitching and cramps, but in the light of subsequent experience the patient was questioned later and described these phenomena intermittently since the start of the illness. Further examination also disclosed brief, 'fibrillary' involuntary contractions in the muscles. As the illness advanced, these twitches increased and were more widespread, including the leg muscles. The leg muscle volume was actually thought to increase under observation but, nevertheless, the patient developed leg weakness.

The 'fibrillary' movements would now be termed fasciculation. The author wonders if the preservation or increase of leg muscle volume, despite weakness and fasciculation, would not indicate corticospinal tract involvement, i.e. amyotrophic lateral sclerosis rather than progressive muscular atrophy. The marked fatigability is also of interest in view of more recent findings which are discussed in detail in the section on electromyography (Mulder et al. 1959; Lambert 1969).

Case 4. A 33 year old man noted weakness of the right arm and fingers about 9 months before hospitalization in 1848. Examination revealed flaccid weakness of the right arm and hand with sparing of the dorsal interosseous muscles. The maximum galvanic current only produced a few fibrillary twitches in the deltoid muscle and the elbow and finger flexors were inexcitable, in contrast to normal contractility in the muscles on the left side. The less weak muscles were excitable but produced weaker contractions. The patient's sensation of these electric shocks was normal. A course of 12 galvanic treatments by Duchenne seemed to result in some improvement in the muscles which were not entirely paralyzed; no change was noted in the completely paralyzed muscles.

Although subject to abnormal fatigability, the patient left the hospital and returned to light agricultural work. He was rehospitalized in March, 1850. His leg strength was good and only the arm muscles refused to serve him. The atrophy of the right hand had progressed to the point where the appearance of the dorsal and palmar surfaces seemed the same. There was no weakness of the left hand. There was forearm involvement, more on the right than on the left, and rare 'fibrillary' involuntary contractions were noted in the right forearm. The right triceps muscle remained normal in the face of severe biceps paralysis. The left arm and shoulder were now affected.

During the interval between the first examination and the follow-up, the patient evidently experienced remission of the leg weakness while there was further progression in both arms. Aran also suggested that there was compensatory hypertrophy of the uninvolved arm muscles, and pointed out that the enlargement of these muscles contrasted with the atrophic appearance of the other muscles.

Case 5. A 28 year old woman, who had suffered intermittently from abdominal pain, developed weakness of the right hand. The weakness increased and this hand became more sensitive to cold than the left hand. Wasting of the muscles developed in the second year of the illness, in the forearm as well as the hand. Although the weakness increased from

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day to day, she courageously continued her work as a dressmaker until she could no longer hold the needle. Typhoid fever occurred 2 years from the onset of paralysis; the convalescence required about 3 months, during which the weakness and atrophy increased and spread to the left arm, again commencing in the interosseous muscles. Muscle twitching and cramps were noted. She was forced to give up her place as a domestic servant because of weakness and entered 'la Charité'.

The general examination seemed to be quite normal, and strength and sensation were normal in the legs. She wept as she displayed her arms with the severe weakness and wasting of the right forearm and hand. Slight movements were evoked in some of the paralyzed muscles by galvanic stimulation, but the majority were not excitable except for faint fibrillary contractions. The less affected forearm muscles and the normal muscles of the shoulder and arm responded normally to galvanism. On the left, the fingers and thumb were continually moving due to small twitching movements within the muscles. The galvanic responses were present, with the strength of contraction reduced proportionate to the muscle wasting. The forearm, arm and shoulder muscles were normal on this side. A course of 12 galvanic treatments resulted in no modification in the atrophic muscles but she felt a little stronger and the involuntary twitches decreased in frequency.

Case 6. A shepherd boy seemed to be normal until the age of 13 years, when he began to masturbate and within 3 or 4 months developed weakness in the legs. This progressed so that at age 15 it was impossible for him to get about without a cane. A striking degree of emaciation occurred in the 9 months before admission to 'la Charité' 3 years later on the service of Cruveilhier. Examination revealed marked wasting throughout the arms, sparing only the finger flexor muscles. He was unable to stand, and could only sit up in bed for a short time. The diaphragm was paralyzed. Galvanic stimulation produced varying degrees of weak or fibrillary contraction, depending on the severity of muscular involvement. The electrical sensation was diminished in the muscles but intact in the skin. A course of galvanic stimulation was begun, and after 4 treatments he showed some improvement but then contracted variola and succumbed. Cruveilhier carried out an autopsy examination and found nothing wrong with the nerve plexuses. The more paralyzed muscles appeared to have been replaced by grey connective tissue.

Duchenne apparently attended the necropsy or studied some of the tissues later, and Aran records that he noted in the other muscles a mixture of grey tissue and discoloration of the muscle fibers. The age of onset makes this a suspect case of progressive muscular atrophy (Table 1).

Case 7. A retired sea captain, who had never had syphilis and had always used venereal pleasures moderately, noted the onset with arm cramps at the age of 43 and died of the disease and concurrent bronchitis at the age of 45. The family history was remarkable because 1 of 3 sisters and 2 maternal uncles apparently died from the same disease. Three brothers and 2 other sisters were still living and showed no symptoms. When the first symptoms appeared in this patient, he was aware of their gravity and undertook most of the treatments available at the time, all without benefit; the atrophy generalized, spreading last to the legs. The onset in each muscle group was heralded by muscle cramps. On examination, he was unable to sit up or turn in bed but if helped to his feet could walk with assistance. The diaphragm was partly paralyzed. Galvanic stimulation produced responses in all the muscles except those which had totally lost voluntary contraction. A course of galvanic treatment was carried out, and after twelve treatments he was able to sit up and turn himself in bed; he also walked more easily. Bronchitis intervened; he was unable to cough up the secretions and at his request was carried home shortly before death.

This patient was probably not seen at all by Aran, who credits Duchenne with providing the data. The rather rapid course of the illness in this case is more indicative of amyotrophic lateral sclerosis than progressive muscular atrophy.

Case 8. Lecomte, an acrobatic clown, entered the hospital at the age of 33 because of an illness which commenced 18 months earlier, shortly after the February Revolution of 1848. Prior to that time, he had managed his own menagerie, which did not require a great deal of vigorous physical work. He had probably suffered from gonorrhea in the past but had good health otherwise. After the political upheaval, he fell on hard times and was forced to reduce his staff and do more and more work himself; he became depressed. After working hard one evening, he awoke with a chill and felt numb in the right side of his body. A short while after, he noticed weakness of the right thumb and index finger, followed by weakness of the entire hand and within 6 months became unable to sign his name. Weakness of the abdominal muscles was noted later that year; he experienced difficulty climbing stairs and felt that his knees were weak. Throughout this time, he noted a peculiar reaction to cold: wristdrop

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developed on the right during exposure to cold and cleared when the arm was warmed. He entered a local hospital and was transferred later to 'la Charité'.

Although intelligence was normal and his memory perfect, his speech was hasty and he stammered. The tongue showed neither weakness, atrophy nor significant tremor. Shaking movements of the arms and sometimes the legs occurred from time to time and there were painful muscle cramps. The right hand was very wasted with the fingers held in chronic flexion (there was good finger flexion strength). Proximally in the arm, there was normal or nearly normal strength. Galvanic stimulation produced faint contractions in some of the hand muscles and relatively normal contractions in the forearm considering some weakness and wasting. The left hand was only slightly affected and had normal electrical responses. The leg muscles were normal in appearance and the patient walked well although he seemed unsure of his footing, more in the evening than in the morning. Electrical stimulation in the legs was normal. A striking finding in the thighs, however, was frequent coarse 'fibrillary' twitching within isolated muscle bundles during relaxation; placing a cold object on the skin increased these involuntary movements, as did passive motion of the limb, or even such stimulation as application of a stethoscope. These twitches occurred also in the relaxed forearm and arm muscles after exertion. A strong contraction of the arm muscles produced similar movements. A variety of treatments including galvanism were undertaken without benefit.

By May, 1850, his condition had become much worse. The right hand was useless and the left hand had progressed to the extent noted previously on the right. His speech was very difficult to understand, the tongue very tremulous. Intelligence remained intact, sensation was normal and there was no difficulty with evacuation of feces and urine. Frequent muscle cramps occurred in the feet when he made any movement in bed. He was intermittently short of breath and there was thoracic muscle involvement, but the diaphragm still appeared to have useful function.

The alterations of strength with cooling and warming were noted but not studied. The twitching in the contracting arm muscles may be the first description of contraction fasciculation. The patient was evidently followed up by Duchenne and the next report of the case is the account of Duchenne's remarks to the 'Société médico-chirurgical' (Duchenne 1853). In the meantime, Lecomte developed almost total paralysis and Duchenne, in describing the case to the society, predicted that death was at hand. Lecomte expired on the following day and the report by Duchenne (1853) is a summary of the clinical course and the changes in the muscles. The latter, combined with the progressive loss of excitability to galvanic stimulation during life, led Duchenne to believe that the disease was situated in the muscles. Cruveilhier (1853), however, pointed out that the severe ventral root atrophy was more likely to cause than be caused by muscular atrophy. A further point of interest is the fairly short course and the marked involuntary movements and muscle reactivity, which strongly suggest hyperreflexia, i.e. amyotrophic lateral sclerosis.

Case 9. A robust 45 year old woman was referred to Duchenne who in turn made her case known to Aran. When 7 or 8 years old, she had an illness marked by pain in the right hand followed by wasting, especially of the thenar eminence, and weakness which was increased by exposure to cold. She became accustomed to using her left hand for most activities. After several years, however, the right hand returned to normal and from the age of 12 there was no difference between her hands. For at least 6 or 7 years before Aran's examination, there had been slowly progressive weakness of the right arm and hand. There was no pain on this occasion and exposure to cold did not increase the weakness although it did give rise to unpleasant numbness such as she had experienced in the childhood illness. For 3 years, there had been visible wasting in the right hand, particularly the thenar eminence, resembling that which was present in childhood. The hand developed the same appearance *en griffe* noted in several of the other cases. For an uncertain time there had also been a prickly sensation in the left arm and some weakness of the hand on the left.

Examination revealed more marked wasting in the palmar surface of the right hand. Galvanic stimulation revealed reduced contractions in the wasted muscles. There was some wasting in the left hand, but the proximal muscles seemed to be normal. There was no trace in the arms of 'fibrillary contractions', either during relaxation or after various maneuvers such as forceful and fatiguing efforts, or galvanic stimulation. A short course of galvanism was undertaken without definite result.

This case is unsatisfactory because of the limited involvement and the prominence of numbness in the hand. The childhood illness is difficult to diagnose from the data provided. Aran stated that this case and the following

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cases 10 and 11 were atypical examples of the new syndrome. He chose to include them because they demonstrated the previously unsuspected frequency of amyotrophic problems, as well as the possibility of variations in the clinical picture as given in cases 1–8.

Case 10. Just 8 or 10 days after seeing the above patient with Duchenne, Aran was called about another example of this disease. The new patient was a Belgian shoemaker, age 37, who had been in good health previously except for an illness lasting several months characterized by intermittent fever. Weakness developed rather rapidly in the left arm approximately one year before. He was suddenly unable to hold a candlestick with his left arm flexed and thereafter noted continued weakness particularly in the presence of cold. He soon felt slightly weak in the opposite arm, and he could only use the left hand for 5 or 6 minutes without great fatigue. The patient was positive that these symptoms had developed rather rapidly, quickly plateaued and were not a great deal worse in the meantime, except that each day, on arising, he seemed strong enough but became weaker as the day progressed. Jumping in the muscles during contraction may have occurred in the arm during exertion but the patient had paid little attention to it.

Examination revealed patchy muscular atrophy in the left arm. Hypertrophy of some muscles made the atrophy more notable. Muscle tone was reduced. The general muscle mass in the forearms was reduced and certain muscles were severely wasted. There was a little weakness and wasting in the hand, but apparently not enough to be considered definitely pathological although the patient complained of inability to firmly grip objects between thumb and forefinger. There was perhaps a little deformity in the muscles of the right shoulder but no other detectable abnormality upon examination. Galvanic stimulation produced very strong contractions in the normal or mildly affected muscles and feeble contractions in the most affected muscles. None of the previous patients had shown the following phenomenon noted in this patient: galvanic stimulation did not immediately bring about the maximal response, which only appeared after a series of little fibrillary oscillations over the muscle surface. No responses at all were obtained over the severely wasted muscles. Some of the normal muscles in the right forearm and arm also displayed the delayed response to galvanism noted in the left arm.

The peculiar delayed response to galvanic stimulation is indeed unusual. Could this have been a case of myasthenic myopathy associated with bronchogenic carcinoma, or Lambert–Eaton syndrome?

Case 11. A 38 year old jewel cutter had acquired lead colic from occupational exposure, for which he had attended 'la Charité' 5 times in the previous 2 years. A sixth bout of colic led to hospitalization. Examination revealed weakness and wasting of the right hand dating back 15 months. He had first noted that, if he worked a long time, the hand became numb and on exposure to cold became weak. The atrophy developed later. In the preceding 3 or 4 months, he also noted painful cramps in the legs, some twitching in the muscles of the face and difficulty in speaking. Examination revealed a robust but pale man. There was a slight blue line on the gums. His movements and strength were quite normal except in the right hand. Both the thenar and hypothenar eminences were weak and wasted. There was some difficulty with galvanic stimulation on the palmar surface of the hand because of callouses. Stimulation dorsally produced weak contractions in the weakened muscles. The right arm seemed a little smaller than the left. There was a slight difficulty in speech and he was unable to protrude his tongue steadily. A few twitches were noted in the face from time to time but none in the right arm or hand.

One would strongly suspect this to be a case of lead poisoning rather than idiopathic progressive muscular atrophy or amyotrophic lateral sclerosis. Thus, only cases 2, 4, 5 and 6 seem likely to satisfy modern criteria of progressive muscular atrophy. Unfortunately, examination of the muscle stretch reflexes and plantar responses were not then part of the clinical art, otherwise the probable cases of amyotrophic lateral sclerosis (Cases 3, 7 and 8) would doubtless have been distinguished from progressive muscular atrophy.

One fascinating aspect of Aran's (1850) report is the description of fasciculation. He emphasized that it occurred in both clinically normal and affected muscles during relaxation but that fatiguing contractions tended to increase it. Fasciculation occurred mostly in the arms or thighs, rarely in the hands and face but was seen in the tongue in 2 cases. Aran recommended the galvanic stimulation employed by Duchenne as an objective test of muscle function. It was possible to demonstrate at least weak galvanic contractions in some muscles which had seemed totally paralyzed.

At risk of undue repetition, more of Aran's (1850) deductions and conclusions, may be summarised, because they remain valid today and further define the clinical picture. He em-

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