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REVIEW

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Diagnosis of acute neuropathies

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Abstract Acute and subacute polyneuropathies present diagnostic challenges since many require prompt initiation of treatment in order to limit axonal degeneration and since an exact and detailed diagnosis is a prerequisite for making the correct choice of treatment. It is for instance of utmost importance to recognize whether the underlying pathological changes are due to demyelination or to axonal degeneration and electrodiagnostic tests can thus in most cases contribute considerably to the securing of an exact diagnosis. The specific and characteristic electrophysiological findings in the different types of acute and subacute neuropathies are discussed, and the various electrophysiological pitfalls and technical problems, which are met in these patients, are mentioned.

Key words polyneuropathy · electrophysiology · nerve conduction studies · sensory nerve · motor nerve

Introduction

Polyneuropathy may be classified according to the temporal development (acute, subacute, chronic); the anatomical distribution of involvement (cranial nerves, upper or lower limbs, respiratory muscles, symmetrical or asymmetrical involvement); functional selectivity (sensory, motor or autonomic fiber affection or combinations of these); the pathological changes (primary affection of myelin or axons); and the underlying cause of the disease (immunological disorder, cancer, infection, toxins, metabolic disorder, or hereditary disease) [13, 31, 110, 145]. The acute and subacute polyneuropathies present a particular diagnostic challenge since these disease states may be treatable and require prompt initiation of treatment.

The aim of this overview is to describe the acute and subacute neuropathies and in particular the characteristic diagnostic findings of these diseases.

Definition of acute polyneuropathy

Acute inflammatory polyneuropathies in Guillain-Barré syndrome are defined as reaching nadir in less than 4 weeks and often within days [8]. A subacute neuropathy is defined as a neuropathy that reaches its clinical maximum in less than a few months (but more than 4 weeks), and forms an ill defined transition between acute and chronic neuropathies that develop over many months to years.

Mononeuropathy due to compression, ischemia or bleeding into the nerve may develop within minutes to hours. In this connection, the autoimmune asymmetric neuropathies (mononeuritis multiplex) present a classification difficulty in the sense that each "attack" of one or more nerves can be defined as acute. However, this stuttering course may occur over many months or years, and the disorder may in this respect reach a confluent chronic state of a generalized polyneuropathy. These relapsing neuropathies often present differential diagnostic difficulties and it is important that diagnostic procedures are promptly initiated to make the correct choice

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of treatment with the least possible delay to avoid further destruction of nerve fibers. These neuropathies will therefore be included here. Furthermore, some chronic polyneuropathies may show acute exacerbations and do thus in some cases present considerable differential diagnostic problems (e. g. diabetic amyotrophy, porphyric neuropathies, alcohol related neuropathies). These cases are therefore also included here. On the other hand relapsing inflammatory neuropathy is usually included in the group of disorders classified as chronic inflammatory demyelinating neuropathy (CIDP).

Patients with sequelae after an acute mono- or polyneuropathy are often considered as suffering from chronic disease. This is incorrect if the deficit is due to axonal degeneration that occurred during the acute attack of the disease and represents incomplete or absent regeneration and recovery.

Acute neuropathies can be grouped into three main categories according to the underlying cause of the peripheral nerve affection (Table 1).

Diagnosis of acute neuropathies

The diagnostic procedures used in diagnosing acute neuropathies include history and clinical neurological examination, analysis of spinal fluid, determination of serum antibodies associated with neuropathies, and nerve biopsy for histopathological examination. Electrophysiological studies play a major and decisive role in the determination of the peripheral nerve involvement. Since the treatment of the neuropathies is determined by the characterization of the peripheral nerve involvement electrophysiological studies are often pivotal in the diagnosis of these neuropathies and the basic principles of electrophysiological test will therefore be summarized below.

Electrophysiological studies

The main purposes of electrophysiological studies are determination of 1) the most likely primary pathological changes (such as axonal degeneration or demyelination), 2) whether motor or sensory fibers or both are affected, and 3) the distribution of abnormalities. The methods include nerve conduction studies and electromyography (EMG) (to ascertain the presence of motor fiber loss) [24], and in selected cases sensory evoked potentials (SEP) and transcranial and root magnetic stimulation (MEP) to estimate the symmetry, extent and pathophysiological changes in sensory and motor nerves [142] and involvement of the central nervous system. Repeat studies may be necessary in early or mild cases of suspected neuropathy.

EMG

In the early phase of an acute neuropathy, EMG changes are sparse in terms of denervation activity and the motor unit potentials do not show signs of reinnervation. The most revealing finding is loss of motor unit activity with reduced recruitment or discrete activity at maximum effort in weak muscles; however, this sign does not distinguish between axonal failure and block of conduc-

Table 1 Overview of acute polyneuropathies according to the cause of the disease

Type of acute polyneuropathy	Main etiological groups	Subclassification	Pathology
Primary acute polyneuropathy	Guillain-Barré syndrome	Acute inflammatory demyelinating polyneuropathy (AIDP)	Demyelination (± conduction block) with variable axonal loss
		Acute motor axonal neuropathy (AMAN)	Axonal degeneration of motor fibers
		Acute motor and sensory axonal neuropathy (AMSAN)	Axonal degeneration of motor and sensory fibers
		Miller Fisher syndrome	Mixed axonal degeneration and demyelination
	Nonsystemic vasculitis without other organ involvement		Ischemic axonal degeneration due to vasculitis
Secondary acute polyneuropathy	Secondary to autoimmune and malignant disorders	Connective tissue diseases, polyarteritis nodosa, Wegener granulomatosis, systemic lupus erythematosus, rheumatoid arthritis, Sjögren, cancer	Axonal degeneration
	Secondary to infectious disease	AIDS, neuroborreliosis, hepatitis C	Axonal degeneration
	Secondary to metabolic disorders	Diabetes mellitus	Axonal degeneration
		Uremia	Axonal degeneration and dysfunction
		Acute porphyria	Axonal degeneration
	Induced by toxic substances	Arsenic, amiodarone, vincristine, cisplatin, pyridoxin, disulfiram, gold salts, glue, alcohol, organo-phosphates	Mostly axonal degeneration, amiodarone associated with demyelination

tion due to demyelination. In cases where the study is carried out days to weeks after the acute onset of symptoms, the EMG may show signs of denervation with fibrillation potentials and positive sharp waves. The interval between the lesion and occurrence of signs of denervation varies between a few days up to 2–3 weeks. The shorter the distance between the site of degeneration and the muscle the faster the denervation signs appear [103, 111]. The extent of denervation is an important factor in determining the degree of axonal loss.

Changes in the motor unit potentials occur over weeks after chronic partial denervation reflecting reinnervation of denervated muscle fibers. Reinnervation may occur, 1) as collateral sprouting with reinnervation of muscle fibers from motor axons innervating other, neighboring muscle fibers, and the reinnervated motor units usually have long duration and polyphasic shape, or 2) as regeneration from completely interrupted motor axons with growth from the proximal axon stump. In this severe denervation the first reinnervated potentials may have brief or long duration polyphasic appearance with low amplitude ('nascent' units), and with time after reinnervation and expansion of motor unit territories the motor unit potentials take on the characteristic features of long duration and high amplitude.

Thus it should be realized that EMG signs of chronic partial denervation with evidence of reinnervation is dependent on the time lapse between the lesion and the examination and is not, as such, evidence of a chronic neuropathy.

Nerve conduction studies

The distribution and severity of involvement of motor or sensory fibers or both are ascertained by determination of amplitudes, shapes, and conduction velocities of compound muscle (CMAP) and sensory nerve action potentials (SNAP), respectively. The amplitudes of the CMAP and the SNAP are the result of summation of individual motor unit potentials and of individual sensory fiber action potentials, respectively, and they are influenced both by the number and synchronization of single unit responses. Desynchronization causes reduced summation and the amplitude may in addition become decreased by phase cancellation. In acute neuropathy reduced amplitudes of the CMAP and the SNAP are sensitive indicators of axonal loss. In the later stages of the neuropathy, the amplitude of the CMAP is affected by compensatory collateral sprouting and the deviation from control values therefore depends on the time of study in relation to the nerve disorder. By contrast the SNAP amplitude is not influenced by collateral sprouting thus making this parameter a sensitive indicator of loss of fibers [88].

The distinction between axonal loss and demyelination is based on the relationship between conduction velocity and amplitude of the compound responses. Loss of fast conducting fibers is associated with proportional reduction of conduction velocity, and the response is a measure of conduction along the remaining less affected fibers. By contrast in demyelination the propagation of activity is determined by the effect of the pathological process on conducting fibers. In chronic generalized axonal polyneuropathies the relationship between the diameters of the largest fibers in the nerve and the conduction velocities of the SNAPs correspond to a conversion factor of ~4.5 m/s/μm, whereas the conduction velocity is lower than expected from the diameters of the largest fibers in demyelinating neuropathy [14]. Considerable inconsistencies are, however, often noted between the findings at nerve conduction studies and the histopathological changes at nerve biopsy in multifocal demyelinating or axonal disorders. The explanations for the discrepancies may be: First, the conduction velocity of the SNAP is determined by the fastest conducting fibers in the nerve and if some fast conducting fibers are spared in a heterogeneous demyelinating process, then the response may have normal velocity and low amplitude and suggest that the lesion is primarily axonal in nature [90]. Second, conduction is studied over much longer distances than the transverse sections at histological examination and the two methodologies therefore provide complementary information and cannot be expected to replace one another. Teasing of nerve fibers provide additional information that cannot be obtained in transverse sections (G. Said, personal communication). It has been increasingly recognized that the amplitudes and conduction velocities of nerve provide only limited evidence about the underlying pathophysiology in peripheral nerve disorders. Thus studies of axonal excitability have greatly increased our understanding of abnormalities that are not immediately accessible through conventional approaches [21, 26].

Although demyelination almost never occurs in isolation, it is, however, important to ascertain whether this is the primary pathological lesion both from a differential diagnostic aspect and because the prognosis is more favorable if the main pathological mechanism is demyelination.

Electrophysiological features of demyelination

Demyelination is characterized by reduced conduction velocities that cannot be explained by loss of fast conducting fibers [14, 87]. In order to define criteria (Table 2) that allow electrophysiological diagnosis of demyelinating inflammatory neuropathy, the findings in patients with characteristic clinical features have been used [2, 3, 72]. These criteria should be considered tentative guidelines and take into account the influence of

Table 2 Motor conduction changes consistent with demyelination

NCS Parameters	Albers and Kelly, 1989 [3]	Ho et al., 1997 [72]	Copenhagen values (limits of values that can be explained by axon loss)	
			Upper limbs	Lower limbs
Distal motor latency	> 115 % of UNL (nl amp) > 125 % of UNL (amp < nl)	> 110 % of UNL (nl amp) > 120 % of UNL (amp < nl)	4.5 ms 5.4 ms	6.4 ms 7.7 ms
Motor conduction velocity	< 90 % of LNL (nl amp) 80% of LNL (amp < nl)	< 95 % of LNL (amp > 50 % of LNL) < 85 % of LNL (amp < 50 %)	45 m/s 38 m/s	35 m/s 30 m/s
Focal conduction changes	Temporal dispersion > 10–15 % increased duration. P/D amp ratio < 0.7	Focal temporal dispersion		
F-wave latency	> 125 % of UNL	> 120 % of UNL		

LNL lower normal 95 % confidence limit; *UNL* upper normal 95 % confidence limit; *amp* amplitude of CMAP; *nl* normal. In the right two columns we indicate the limit of motor conduction velocities that can be explained by axonal loss at our laboratory taking strict temperature control into consideration in middle-aged individuals

loss of axons. According to the distribution of motor conduction velocities, the lower limit explained by loss of fibers in the upper limb is about 45 m/s [46, 47] corresponding to 60–70 % of control mean values (Table 2) [143].

Demyelination in acute neuropathy may be associated with *conduction block of motor fibers* (motor conduction block, MCB), defined as a more than 50 % reduction of the CMAP amplitude evoked by proximal as compared with distal stimulation [117]. Sensory conduction block is a rare phenomenon in acute demyelination but has been documented in patients with chronic inflammatory demyelinating neuropathy of the multifocal acquired demyelinating motor and sensory neuropathy (MADSAM) or Lewis-Sumner syndrome [88, 90, 101, 132]. Although conduction velocity across a nerve segment with conduction block is uncertain, measurements usually indicate it to be reduced. MCB is usually accompanied by weakness of the muscles innervated by the blocked nerve, although some reports indicate that MCB may occur in the absence of overt weakness [115], and that the criteria of 50 % amplitude reduction may be too conservative [118, 121]. Slowing of conduction alone does not cause weakness (or sensory loss).

Certain considerations must be made before a conduction block is established: 1) it must be considered unlikely that the amplitude drop is caused by temporal dispersion and phase cancellation due to diminished numbers of motor units contributing to the CMAP [116, 121]. In other words, if the amplitude of the distally evoked CMAP is very small (less than 1 mV) it will not be possible to diagnose a conduction block with certainty. 2) Conduction block may also be confounded with conduction failure in cases with loss of axonal continuity. If the nerve is examined so early in the course of Wallerian degeneration that conduction in the distal nerve stump is still possible conduction block may erroneously be diagnosed. This error occurs in particular in vasculitis and demonstration of conduction block must therefore in doubtful cases be repeated to ascertain whether conduction in the distal nerve stump fails. 3) Certain technical demands must be met before a conduction block is diagnosed: in cases where the nerve at the proximal stimulation site is located deeply (due to normal anatomy, obesity or edema) it must be ascertained that the nerve is stimulated supramaximally. Using surface stimulation it has been advocated that the stimulus strength must be more than four times the strength of the threshold stimulus [98]. This may not always be possible, and in these instances the stimulation may be delivered via a needle placed in close proximity to the nerve. Other methods include the use of high voltage stimulators or special surface electrodes [4, 104].

Electrophysiological features of axonal degeneration

Some axonal loss occurs in nearly all cases of demyelinating neuropathies, but its degree varies widely and may be difficult to ascertain by nerve conduction studies in the acute phase due to temporal dispersion, multifocal conduction block, and in severe cases due to inexcitability of nerve fibers by the stimulus current. The axonal loss, seen as a reduced CMAP, may be localized at any site along the length of the nerve, i. e. a distal localization has the same effect on the CMAP as axonal degeneration at the ventral root. Axonal loss is definitely demonstrated by denervation activity and it is therefore necessary to perform EMG examinations in order to ascertain axonal loss. If the lesion leading to axonal degeneration is very proximal, it may take several days (even weeks) before denervation activity appears and repeated EMG studies may therefore be necessary.

Can electrophysiological studies contribute to the prediction of the prognosis?

The prognosis in Guillain-Barré syndrome depends mainly on the degree of axonal loss and the localization of the lesion leading to the nerve degeneration, and elec-

trophysiological studies are therefore needed in order to be able to predict the prognosis. In general the degree of axonal loss has major impact on the prognosis since recovery depends on nerve regeneration and reinnervation after fiber degeneration, rather than on recovery of conduction after remyelination. Thus repeated nerve conduction and EMG studies may be required in order to predict the loss of nerve fibers. Recovery is, however, relatively rapid when the localization is distal due to the short regeneration distance as it occurs in some cases of acute motor axonal neuropathy (AMAN). It may be impossible to ascertain if the lesion is localized distally or proximally, but in the case of combined prolonged distal latency, severely diminished CMAP, and a normal proximal conduction velocity, the lesion is most likely distal. Early denervation activity in the muscle(s) also suggests that the lesion is distal.

Acute primary neuropathies

This category includes disease states where the only primarily affected structures are the peripheral nerves, and comprises the four subclasses of inflammatory neuropathies included in the Guillain-Barré Syndrome (GBS) and some cases of systemic vasculitis (Table 1).

The GBS was previously regarded as a single entity characterized by demyelination of proximal as well as distal segments of the peripheral nerve system. It is now generally accepted that the neuropathy has different manifestations.

Etiology

The pathogenesis of GBS is unknown, but infectious disease precedes the disease in 60–70 % of cases and an immunological cross-reaction (molecular mimicry) is suspected as part of the pathophysiological mechanism. It seems probable that the different manifestations are triggered by different pathogenetic epitopes as also supported by animal models of the disease [140]. The majority of GBS patients have had an antecedent respiratory infection with cytomegalovirus (CMV), Epstein-Barr virus, Mycoplasma pneumoniae or Haemophilus influenzae [78]. A preceding Campylobacter jejuni gastrointestinal infection in GBS patients has been established in 14 % to 66 % of cases included in case-control studies [60] and this microorganism has been linked especially to the subclass of GBS with AMAN. The immunological profile in AMAN is characterized by high incidence of IgG GM1, GM1b and GD1a antibodies, which is different from the profile seen in AIDP but similar to that seen in AMSAN patients [157]. The antibody profile was associated with specific pathophysiological changes: in patients with raised anti-GM1 antibodies the motor response was reduced, whereas in patients with anti-GQ1b the sensory response was absent or reduced [77]. Nevertheless, since only a minority of the infected patients develop GBS, host factors influencing the patient's immune response may also play a role. GBS has been found more frequently than could be explained by chance in patients with HIV infection [30, 69, 106], and has also been described in lymphoma, Hodgkin's disease, graft-versus-host reaction after allogenic bone marrow transplantation, and other types of cancer.

Clinical features

GBS is characterized by ascending weakness and sensory disturbances (sensory loss, paresthesia) and loss of tendon reflexes. The onset of symptoms is sudden and may evolve rapidly to reach a maximum within a few days. If progression continues after four weeks the diagnosis must be reconsidered. The symptoms may progress to paralysis and respiratory failure and there may be cranial nerve involvement. Many patients complain of severe pain in arms and legs. During the acute phase cardiac rhythm disturbances and fluctuation of blood pressure may be pronounced due to involvement of the autonomic nervous system.

Diagnosis of GBS

The diagnosis of GBS is in the acute phase primarily based on defined clinical criteria which include symmetrical, ascending weakness, loss of reflexes, and a progression that does not extend beyond 4 weeks [8, 11, 12].

Laboratory findings

Supportive laboratory findings include raised spinal fluid protein and less than 10 leukocytes/ml [50]. If the leukocyte count is raised above this limit, underlying neuro-borreliosis, sarcoid or HIV may be suspected [30, 99, 119, 131]. The protein content in the spinal fluid may not be raised until 10 days after onset of disease and lumbar puncture may need to be repeated if the diagnosis remains doubtful.

Electrophysiological studies in GBS

Nerve conduction studies play a pivotal role in the diagnosis of GBS. The particular electrophysiological abnormalities found in each subclass of GBS will be described separately.

Acute inflammatory demyelinating neuropathy (AIDP)

AIDP is the most frequent subtype of GBS in Europe and the United States and affects persons of both genders and all ages.

Electrophysiological studies in AIDP

The disease is multifocal and electrophysiological study may show varying abnormalities in different nerves [108]. Although demyelination directly affects conduction, other factors including inflammatory mediators and cytokines may affect the excitability and function of nerve fibers [137]. Some nerves may show normal conduction and the electrophysiological studies of several motor and sensory nerves are required to ascertain the diagnosis. The proximal-distal distribution of changes along the individual nerve shows considerable variability. Some patients have mainly distal prolongation of the motor latencies and reduced sensory conduction velocities, whereas others show mainly or exclusively proximal abnormalities (Fig. 1). The axonal excitability measured at the wrist was in one study normal suggesting that the changes in conduction were distal to the site of study [96]. In cases with predominant root involvement, abnormalities are primarily evident in prolongation of the F-wave latencies or by the latency of magnetic evoked potentials (MEP) evoked by root stimulation. Finally other patients have widely distributed changes (Fig. 2 and Fig. 3). It should, however, be realized that some patients have few or no changes when tested early in the disease [150], and in cases with mild clinical involvement electrodiagnostic findings may be few and uncharacteristic [62]. Thus the electrophysiological examination should be repeated if the diagnosis remains unclear or the symptoms do not respond to the treatment (Fig. 3).

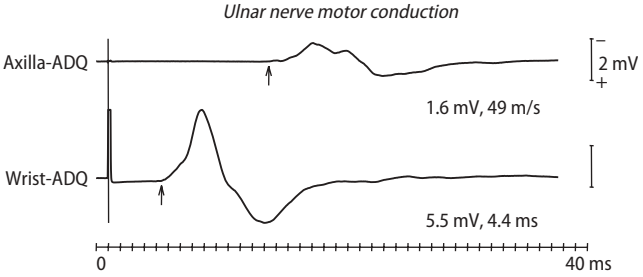

Fig. 1 Motor conduction block in 54-year-old male with Guillain-Barré syndrome. The amplitude of the compound muscle action potential evoked at the axilla was 71 % lower than the amplitude of the response evoked at the wrist. The distal motor latency was 46 % prolonged and the conduction velocity was 21 % reduced

Acute motor axonal neuropathy (AMAN)

This variant of GBS is characterized by hyperacute onset of paresis/paralysis (often with the need of artificial respiration) and absence of sensory disturbances. The spinal protein is raised without increased cell count and the disease is usually, but not always, accompanied by a

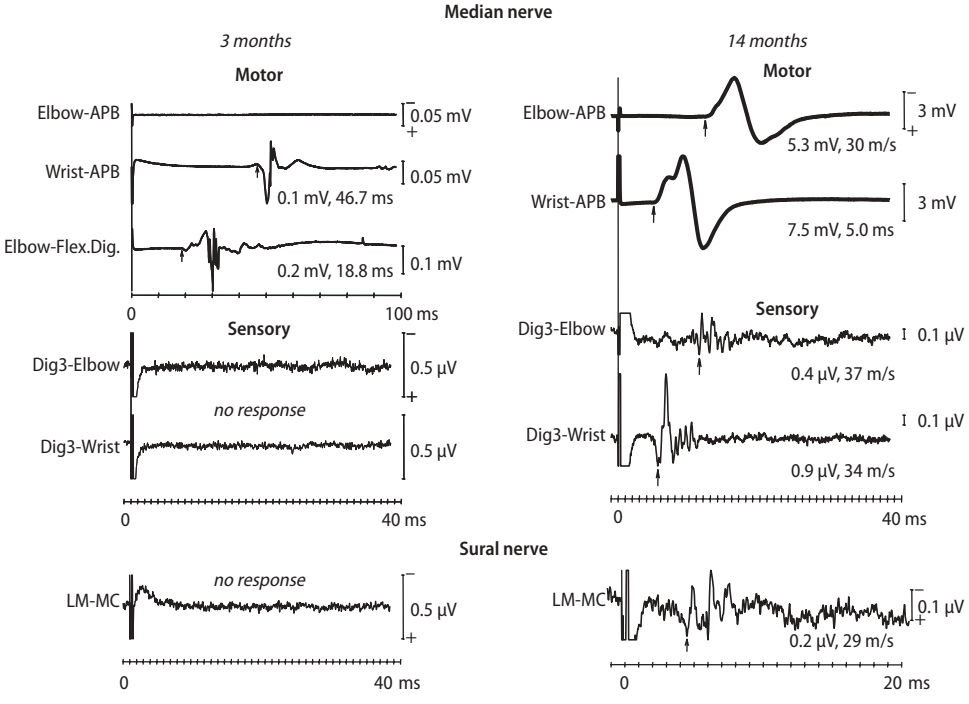

Fig. 2 Loss of excitability of peripheral nerves in 68-year-old with severe Guillain-Barré syndrome. He had tetraparalysis, sensory loss and was dependent on mechanical ventilation. EMG showed absent voluntary activity and severe denervation activity. The median nerve showed only minimal motor responses with severely prolonged latencies and no motor responses could be recorded from the lower extremities (peroneal nerve). Sensory responses were absent from the median and sural nerves. At 14 months after presentation the patient could walk. Conduction studies at this time showed normal amplitudes of the compound action potential from the abductor pollicis brevis muscle. The sensory action potentials evoked at digit 3 showed reduced amplitudes. Motor and sensory conduction velocities were reduced. The sensory potential in the sural nerve had markedly reduced amplitude and conduction velocity. The findings indicated that the initial loss of excitability was due to demyelination and that the subsequent recovery was due to remyelination as well as to reinnervation

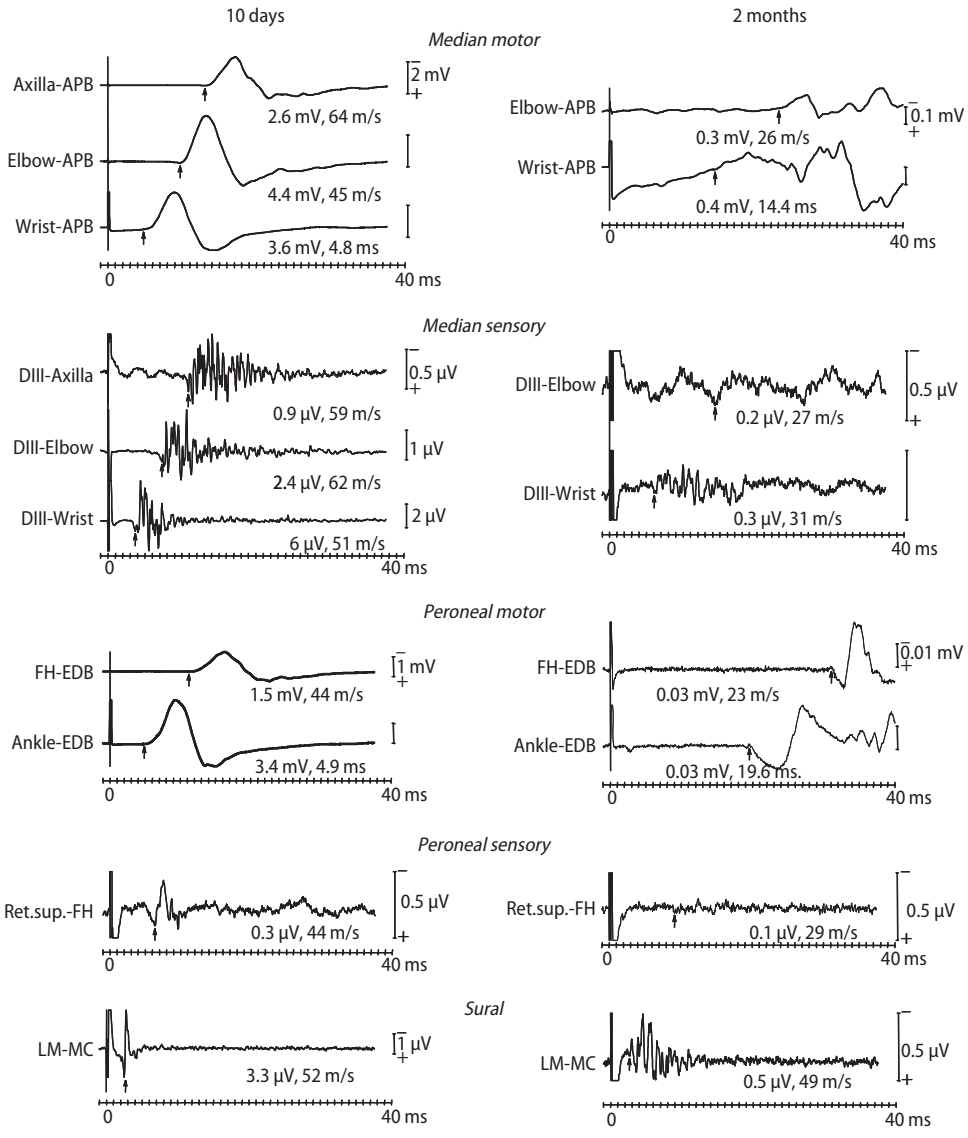

Fig. 3 Progressive clinical and electrophysiological abnormalities in 54-year-old man with Guillain-Barré syndrome after upper respiratory tract infection. At 10 days after presentation the patient had distal and proximal weakness in the arms and legs, distal numbness and absent reflexes. Spinal protein was normal, and there was some improvement at plasma exchange. Conduction studies showed mild distal slowing of motor conduction velocity and markedly dispersed sensory potentials in the median nerve, motor conduction block and reduced sensory amplitude in the peroneal nerve, and reduced amplitude of the sural nerve action potential. Following plasma exchange symptoms progressed despite treatment with IVIg and the patient became non-ambulatory with severe tetraparesis at 6 weeks after the first study. At this time conduction studies showed marked progression of motor and sensory abnormalities of the median, peroneal and sural nerves. Distal motor latencies became markedly prolonged and amplitudes of both motor and sensory responses decreased by more than 90 %. From Krarup, 2004 with permission

loss of reflexes. Particularly at the onset of the disease the tendon reflexes may be retained or even hyperactive, which in some cases lead to doubt about the diagnosis [94, 95]. This subclass of GBS was originally described in China in many cases with relatively fast complete or partial recovery [66, 72, 107]. In Western Europe and the USA, it is much rarer, and the prognosis poor. Poliomyelitis may in some areas be a differential diagnostic possibility, but it can be considered an unlikely diagnosis if not accompanied by meningitis. *C. jejuni* infection (with subsequent production of IgG antiganglioside antibodies GM1) is thought to trigger the illness in many cases. Mycoplasma infection has also been found to precede the disease in some cases [141]. Both in patients with AMAN [66] and in the animal model of the disease [140, 158] the pathology is characterized by periaxonal macrophage attack with antibodies and activated complement deposits on the axon membrane.

Electrophysiological findings

Motor nerve conduction studies show axonal loss without signs of demyelination, and sensory nerve conduction studies are normal (Fig. 4). EMG studies show profuse denervation. Excitability studies in AMAN have shown abnormalities localized to the distal segment of motor fibers [96], which is consistent with rapid recovery probably due to regeneration.

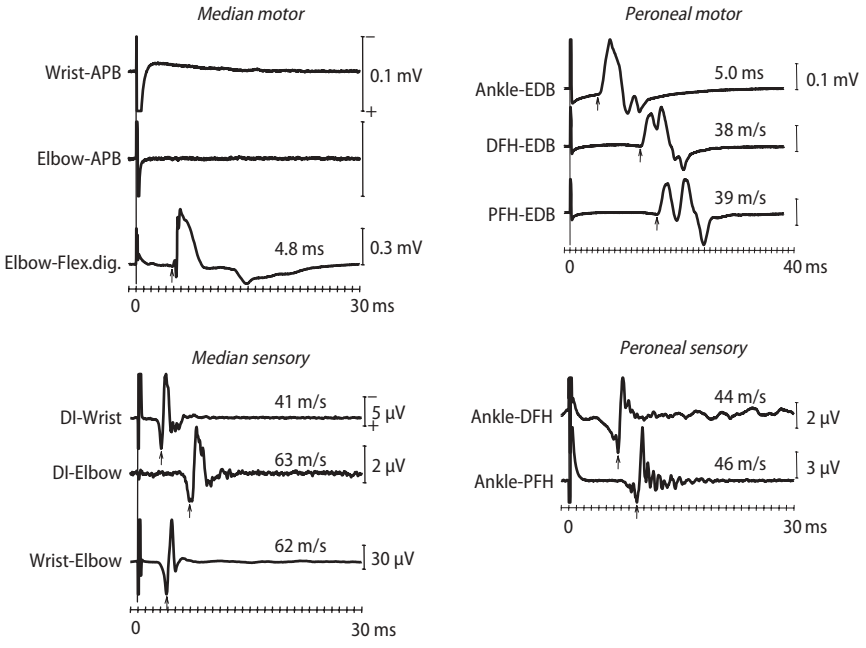

Fig. 4 Progressive severe distal and moderate proximal weakness of the upper and lower extremities without sensory loss and without respiratory symptoms in 46-year-old man with acute motor axonal neuropathy (AMAN). Loss of reflexes, and spinal protein was 94 mg%. EMG of distal muscles of the hands and legs showed pronounced denervation activity and absent voluntary activity of the abductor pollicis brevis and abductor digiti quinti. Conduction studies showed absent motor responses in the APB and severely reduced amplitude of flexor digitorum muscle. The sensory responses from digit 1 (DI) and the mixed nerve action potential from elbow were normal. The amplitude of the motor response from the extensor digitorum brevis (EDB) was severely reduced whereas the sensory potential from the peroneal nerve was normal. From Krarup, 2003 with permission

Acute motor and sensory axonal neuropathy (AMSAN)

Some patients with hyperacute GBS develop flaccid tetraparalysis, respiratory distress and sensory disturbances over 1–4 days, and show signs of primarily axonal motor and sensory fiber degeneration [23, 51, 52]. These cases may be considered as representing a severe form of AIDP where the axonal degeneration is a result of severe demyelination, and pathological studies have in some of these patients shown axonal degeneration as well as severe demyelination [56]. However cases of severe GBS with a hyperacute onset and pronounced signs of nerve fiber degeneration are categorized as belonging to the subclass AMSAN of GBS.

Electrophysiological findings

Motor and sensory nerve conduction studies show severely reduced CMAPs and SNAPs as signs of axonal loss and EMG studies show profuse denervation activity. Furthermore the motor fibers may in these patients be inexcitable [23, 52]. Although this is consistent with axonal loss, it should be remembered that severe demyelination may also render fibers inexcitable (Fig. 2).

Miller Fisher syndrome (MFS)

This syndrome, which occurs in 6–7 % of patients with GBS, consists of acute onset of extraocular ophthalmoplegia, ataxia, loss of reflexes with raised spinal fluid protein content, and usually rapid and complete recovery [53, 113]. The disorder is heterogeneous and may involve sensory loss and widespread weakness [82, 151]. The disorder is often preceded by respiratory symptoms or by enteritis, and particular attention has been focused on the relationship with *Campylobacter jejuni* infection [152]. IgG anti-GQ1b and anti-GT1a antibodies have been found in serum of 80–100 % of patients with MFS [5, 29].

Electrophysiological findings

Nerve conduction studies are variable in MFS. Sensory nerve conduction studies have shown peripheral nerve involvement [67] with recovery in serial studies [79, 80]. Axonal loss and demyelination may be found if several nerves are investigated [54]. Some cases show severe involvement of sensory fibers [136]. In rare patients with tetraparesis nerve conduction studies showed only slightly reduced amplitudes of the CMAP suggesting a different pathophysiology from that seen in AIDP [82].

Acute and subacute neuropathies secondary to other diseases

This category includes polyneuropathies secondary to cancer, immunological disorders, and severe disease courses with sepsis and multiorgan involvement, diabetes, diphtheria and HIV infection.

Neuropathies secondary to cancer and immunological (autoimmune) disorders

These neuropathies can subacutely affect sensory fibers or sensory ganglion cells only while leaving motor fibers intact and are then categorized as subacute sensory neuropathies (SSN). SSN usually develops over a few weeks to months, but can sometimes develop over days and may also occur in a more chronic variant [9, 73]. SSN with characteristic clinical features may be caused by a number of systemic disorders and be the result of toxic substances [135].

Clinical features

SSN is characterized by sensory loss, paresthesiae, and pain often in an asymmetrical distribution, starting in the upper or lower limbs [28]. The disorder may progress to involve all four extremities and even the trunk and face, and may render the patient so severely ataxic that unsupported movements are impossible and pseudoathetosis may develop. Muscle power is usually not affected though the patient due to ataxia may have so little voluntary control that strength is difficult to test. Tendon reflexes are lost in a pattern according to the sensory loss. The prognosis is poor regarding the sensory neuropathy especially when the disease is caused by degeneration of dorsal root ganglion cells precluding recovery by regeneration. Although SSN is the most characteristic type of neuropathy in cancer, patients more frequently present with a mixed sensory and motor neuropathy, which may show axonal or demyelinating features [27, 89], and paraneoplastic neuropathies usually take the form of a generalized neuropathy [36, 37]. In paraneoplastic SSN, the patients may not have symptoms of the underlying malignancy at the time of presentation, and they may show additional signs of CNS involvement with encephalomyelitis or limbic encephalitis.

Etiology

The pathophysiological mechanism of neuronal degeneration in SSN is not clear. In connection with malignant disease (especially small-cell lung carcinoma, breast and ovarian cancer) [7] and Sjögren disease [61, 105, 112] the neuropathy is considered an autoimmune manifestation, and the nerve tissue is infiltrated by mononuclear cells [42]. Nevertheless, in some cases no underlying disease can be found. In small cell lung cancer antibodies against neuronal nuclear antigens (ANNA1, anti-Hu) are present in the blood and the CSF [6, 27, 35, 89, 100]. In other types of cancer some patients have shown presence of anti-Purkinje cell antibodies (PCA-1, anti-Yo). Antibodies to extractable nuclear antigens (ENA), such as SSA-Ro and SSB-La, have been found in patients with Sjögren syndrome and peripheral neuropathy and could be useful serologic markers to support the diagnosis [65, 114]. Patients with Sjögren syndrome may in addition to SSN have a distal symmetric sensorimotor neuropathy and trigeminal sensory neuropathy [59, 65, 74, 81]. The CSF shows raised protein and cells in patients with SSN secondary to cancer [43, 109] and in some with Sjögren disease [42, 112].

Electrophysiological findings

SSN are characterized by loss or severe reduction of the SNAP whereas EMG and motor nerve conduction studies indicate a normal peripheral motor system.

Neuropathies associated with systemic disorders with arteritis (vasculitic neuropathies)

Vasculitic neuropathies are seen in association with polyarteritis nodosa (PAN), rheumatoid arthritis, Churg-Strauss syndrome, Sjögren disease, systemic lupus erythematosus (SLE), as a paraneoplastic manifestation, and in patients with HIV [22]. In some cases (up to one-third of patients) [85], no underlying systemic disease can be detected [38, 64, 86, 129]. Nevertheless, the fact that muscle biopsy often reveals vasculitic changes indicates that the underlying pathology is not confined to peripheral nerve. Vasculitis causes peripheral nerve involvement in an acute, subacute or chronic pattern [70, 86, 128, 138]. Recognition of vasculitis as the cause of peripheral neuropathy is important since the disorder is treatable. The diagnosis is straightforward in cases of known systemic vasculitides but should also be considered in patients who present with a sudden onset neuropathy, but who otherwise seem healthy, since the neuropathy may be the first or only clinical manifestation of vasculitis.

Clinical features

A vasculitic neuropathy is usually characterized by a focal onset of symptoms, and may be restricted to one toe or one finger, which indicates that a single nerve or fascicle may initially be involved. Mononeuritis and mononeuritis multiplex may progress further in a stuttering manner in parallel with the involvement of individual peripheral nerves, in particular the peroneal, tibial, ulnar and median nerves unilaterally or bilaterally. At late stages a confluent mononeuritis multiplex with features of a polyneuropathy may be reached. However, in some cases the neuropathy develops gradually or rapidly in a symmetrical fashion [128].

Etiology

Necrotizing angiitis is the etiological factor in most cases and the pathogenetic mechanism is ischemia of nerve fibers, which causes Wallerian degeneration. In some cases of lymphoma an angiopathy (with invasion of malignant cells in some cases) without necrosis may be observed. In a proportion of patients, the CNS in addition to the PNS may be involved (e. g. SLE).

Neuropathy frequently occurs in multisystemic disorders due to necrotizing arteritis in polyarteritis nodosa (including Churg-Strauss syndrome with eosinophilia), rheumatoid arthritis, SLE, Sjögren syndrome, Wegener's granulomatosis with positive antineutrophil cytoplasmic auto-antibodies, ANCA. Patients with SLE may rarely develop a GBS-like syndrome, however, characterized by axonal loss, and raised spinal fluid protein and cells. In addition, necrotizing vasculitis may be seen in neuropathy in patients with HIV infection and in hepatitis B and C [22, 34, 55, 58, 99, 123]. Isolated vasculitis neuropathy is primarily seen in the elderly. Vasculitis may occur in association with gammopathy.

Mononeuropathy due to other causes occurs in diabetes mellitus, primarily localized to the proximal nerves of the lower limbs (neuralgic amyotrophy) either as an isolated manifestation of DM or on the background of a generalized diabetic sensorimotor neuropathy. In these cases, vasculitis has also been demonstrated in some patients [129, 130].

Electrophysiological features

EMG and nerve conduction studies in all types of vasculitic neuropathy show evidence of axonal loss. If the patient is examined in the acute stage, nerve conduction studies may show features suggesting conduction block without or with minimal conduction slowing. This is, however, due to evolving Wallerian degeneration where conduction can still occur distal to the site of focal ischemia and loss of axonal continuity (Fig. 5). Both motor and sensory fibers are involved, and there are signs of denervation in EMG studies.

Patients with involvement of peroneal, ulnar or median nerve affection present with symptoms similar to peroneal palsy, ulnar nerve entrapment or carpal tunnel syndrome (Fig. 6). It is therefore essential that the nerve conduction study be carried out to exclude focal compression at these sites. Nevertheless, the electrophysiological studies do not show evidence of median nerve compression indicating that the mononeuropathy is not due to entrapment (Fig. 6). It is often revealing to carry out conduction studies in the same nerves bilaterally, e. g. sural, peroneal, ulnar or median nerves, to show asymmetry.

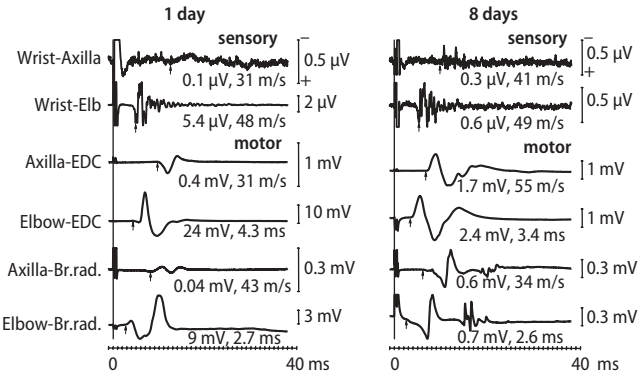

Fig. 5 Conduction failure associated with Wallerian degeneration in 86-year-old man with mononeuritis multiplex and vasculitis. The patient suddenly developed right wrist drop. On day 1 conduction studies of the radial nerve showed a moderate 75 % reduction of the sensory action potential (SNAP) amplitude at the elbow with normal conduction velocity. At the axilla the SNAP was severely reduced and conduction between elbow and axilla was slowed. The amplitudes and latencies of the compound muscle action potentials (CMAP) in the extensor digitorum communis (EDC) and brachioradial (Br.rad.) muscles from the elbow were normal, whereas the amplitudes from the axilla were markedly decreased and the motor conduction velocities between axilla and elbow were reduced. Although motor and sensory conduction block was suspected, repeat conduction studies on day 8 showed that the apparent conduction block was due to axonal failure: the amplitudes of the SNAP and the CMAP at the elbow had decreased by about 90 % compared to day 1 and were similar at elbow and axilla indicating axonal degeneration

Histopathological studies

Morphological studies from nerve or muscle or both must be carried out to show characteristic lesions, in particular in non-systemic or doubtful cases. It is advised that studies are carried out both on nerve and muscle specimens to demonstrate vasculitic lesions characterized by transmural infiltration of polymorphonuclear cells, lymphocytes and eosinophils, fibrinoid occlusion of the lumen and sparing of venules [128]. Due to the focality of these lesions serial sections must be studied, and the absence of vasculitic lesions does not exclude the diagnosis. Nerve biopsies show pronounced fiber loss, often in a patchy distribution affecting some fascicles more than others.

Critical illness neuropathy

The acute or subacute paresis which develops in intensive care unit patients with sepsis and multisystem involvement has become increasingly recognized as a serious complication [17, 18, 39, 57]. The etiology of the disorder is unclear but its development is related to the extent of organ failure, and the use of corticosteroids and non-depolarizing neuromuscular blocking agents [19, 75]. This entity has features that make it distinct from Guillain-Barré syndrome [20, 41], though electrophysiological differentiation between the axonal variant of GBS and the axonal degeneration that occurs in criti-

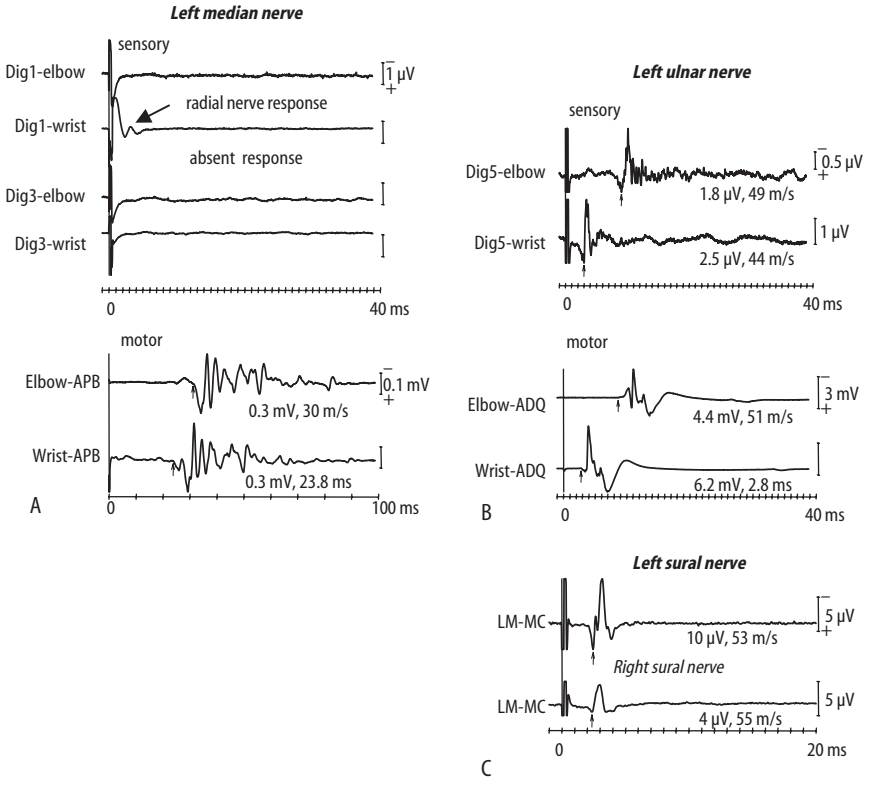

Fig. 6 Median and ulnar nerve conduction studies in 75-year-old woman with clinical and electrophysiological signs of mononeuritis multiplex. The patient developed severe weakness of the right arm, the left hand and of both legs, left more than right, after severe streptococcus infection 2 months before the electrophysiological study. **A** Severe motor and sensory fiber loss from the left median nerve. The prolonged latency and reduced conduction velocity of the compound muscle action potential (CMAP) from the abductor pollicis brevis muscle (APB) was due to regeneration after complete degeneration. SNAPs were absent from both digit 1 and digit 3. The small SNAP recorded at stimulation of digit 1 (arrow) originated from the radial nerve. **B** Mild motor and sensory fiber loss from the left ulnar nerve was indicated by the slight amplitude reduction in the abductor digiti quinti (ADQ). The SNAP evoked at digit 5 was normal. **C** Asymmetrical sensory fiber loss with reduction of the SNAP from the right sural nerve. From Krarup, 2004 with permission

cal illness neuropathy may be difficult. The pathophysiological mechanism is unclear and it is even doubtful whether the disease entity which in many cases is designated critical illness polyneuropathy (CIP) is a true neuropathy, a neuro-myopathy (CIMP) or a myopathy (CIM).

Clinical features

The diagnosis is considered when the patient cannot be weaned off the ventilator, and is then found to be tetraparetic/tetraparalytic often with absent reflexes. Sensation is usually spared though a reduced level of consciousness hampers the clinical examination, and a differential diagnosis of GBS is often considered [41]. Nevertheless, critical illness neuromuscular disease occurs while the patient is in the intensive care unit, whereas most patients with GBS are admitted to the ICU with severe weakness. The weakness is considered to be due to axonal degeneration or to myopathy or to both in combination. The extent of muscle involvement as compared with nerve fiber involvement is, however, uncertain.

Electrophysiological findings

The electrophysiological examination must frequently be carried out under difficult conditions at the bed-side, and should include EMG as well as both motor and sensory nerve conduction studies if possible, since the electrophysiological picture in this disease is complex. The sensory nerve conduction is often normal or only slightly affected, while the motor conduction studies often show CMAPs of decreased amplitude (Fig. 7), prolonged duration and normal to moderately reduced motor conduction velocities [19, 120]. The EMG-examination frequently shows profuse denervation activity in weak muscles. Recording of motor unit potentials (MUPs) requires that the patient can cooperate to generate weak contraction and may often be impossible to obtain in patients with concomitant encephalopathy. When MUPs can be recorded, they may show evidence of myopathy with short duration and increased incidence of polyphasic potentials, and at maximal effort low amplitude recruitment pattern (Figs. 7 and 8). Diagnostic criteria for critical illness myopathy (acute quadriplegic myopathy) [17, 68, 76, 122, 147, 153], have been proposed [97] to include normal SNAP (taking the presence of edema into consideration by recording with a needle electrode if needed [19]), evidence of myopathy on EMG and muscle biopsy and excluding other disorders such as Guillain-Barré syndrome and neuromuscular transmission disorders. Direct stimulation of muscle (Fig. 9) has been proposed to add significantly to the diagnostic certainty [124, 147] by showing reduced excitability of the muscle fiber membrane [125, 126]. In

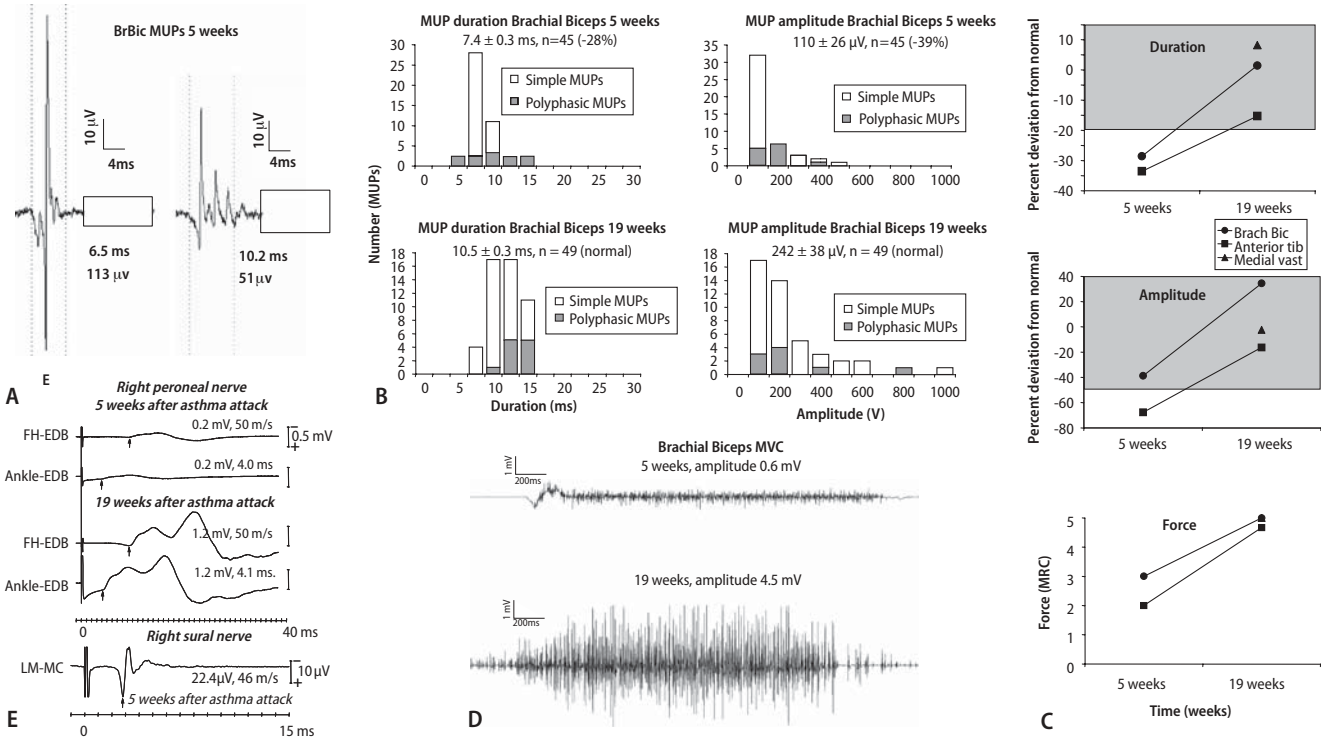

Fig. 7 Acute quadriplegic myopathy in 24-year-old woman after severe asthma attack treated first on heart-lung machine and then mechanical ventilator. She was tetraparalytic with normal sensation and absent reflexes at 5 weeks after asthma, and then gradually recovered. **A** Examples of short duration and low amplitude MUPs from the Brachial Biceps muscle at 5 weeks. **B** (left column) The duration of Brachial Biceps MUPs at 5 weeks was markedly shortened, and at 19 weeks normal; **B** (right column) the amplitude was borderline reduced at 5 weeks and recovered at 19 weeks. **C** The duration, amplitude and force recovered partially or completely between 5 and 19 weeks after the asthma attack. Shaded areas of the MUP duration and amplitude indicate normal ranges. **D** Recruitment pattern in the brachial biceps muscle during maximal voluntary contraction at 5 weeks, with markedly reduced amplitude, and 19 weeks, with normal amplitude after asthma. **E** Markedly reduced amplitude of the compound muscle action potential recorded from the extensor digitorum brevis muscle at ankle and fibular head stimulation of the peroneal nerve with partial recovery of the response from 5 to 19 weeks after the asthma attack. The sural nerve sensory action potential amplitude and conduction velocity were normal

this respect myopathy in critical illness differs from the membrane function in e. g. muscular dystrophy where the muscle fiber conduction velocity is normal [25]. Recovery of muscle force is accompanied by normalization of the CMAP at stimulation and of the MUP parameters at EMG (Fig. 7). Muscle pathology is often less pronounced than that expected considering the amount of denervation activity. For example in myositis and muscular dystrophy, denervation activity occurs in about half the patients [25] and is proportional to the muscle fiber destruction and the creatinkinase level in serum [49, 146, 149]. In critical illness the muscular involvement has been classified as being due to (for review, see [19]): loss of thick filaments, necrotizing myopathy or "cachexic" myopathy.

The distinction of CIM from CIP may be difficult in the patient with abundant denervation activity, small amplitude CMAP and short duration MUPs (Fig. 8) [148, 156, 159] and only small changes in nerve conduction studies. Short duration MUPs may occur in terminal branch axonal degeneration, proposed to occur in CIP studied by single fiber EMG [134]. The diagnostic criteria for CIP [19] include reduced amplitude SNAP as well as CMAP in the setting of axonal degeneration (Fig. 9). The presence of MUPs consistent with myopathy in some muscles and with neurogenic abnormalities in other muscles (Fig. 8) may suggest that patients may have signs of combined critical illness myopathy and polyneuropathy (CIMP).

Differentiation from GBS must be sought by performing a lumbar puncture. Spinal fluid examination in critical illness neuropathy is normal as opposed to GBS. Nerve biopsy examination shows axonal degeneration without inflammation.

Etiology

The pathogenesis in critical illness neuropathy is unknown but cytokines (e. g. TNFα) are considered [32, 32, 33] to play a role, and activation of local immune mechanisms have been suggested [40, 155]. The muscle fiber involvement in CIM has been suggested to be due to apoptosis [44, 45].

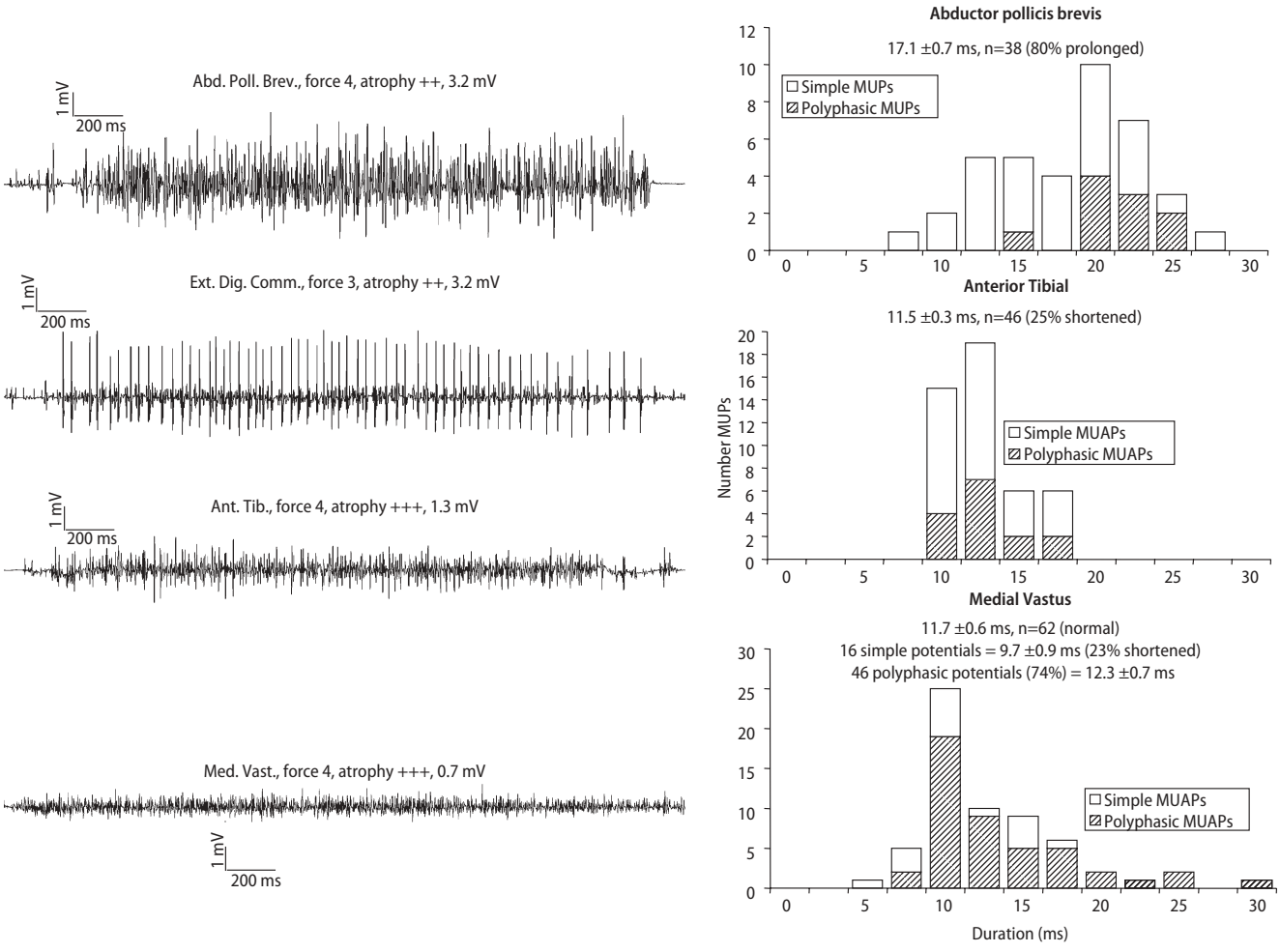

Fig. 8 Critical illness polyneuropathy (CIP) in 74-year-old man with history of intestinal surgery followed by leakage, peritonitis and septic shock, intubated and mechanically ventilated for two months before examination. He had paralyzed legs and weakness of the arms, no bulbar symptoms. No sensory symptoms. On examination severe distal weakness in the distal more than the proximal legs, moderate weakness in the distal upper extremities. No sensory loss. Reflexes in the arms weak, in the legs absent. Left panels maximal voluntary force of the right abductor pollicis brevis showed slightly reduced pattern of normal amplitude, discrete pattern in the extensor digitorum communis muscle, and reduced to full recruitment patterns of severely reduced amplitude in the Anterior Tibial and Medial Vastus muscles. These findings in the APB indicated chronic partial denervation and the MUP duration was prolonged, also consistent with neurogenic changes. In the legs the recruitment pattern indicated myopathy, and the shortened MUP duration of the Ant.Tib. and the Med.Vast. was consistent with this

Neuropathies secondary to metabolic disorders

Acute neuropathies associated with diabetes mellitus (DM)

DM is associated with several syndromes involving the peripheral nervous system, most of which are chronic. There are, however, some distinct acute focal and multifocal clinical entities (1 and 2) and an acute symmetric neuropathy [3] associated with diabetes.

1) Lumbosacral radiculoplexus neuropathy/diabetic neuropathy/diabetic amyotrophy most often afflicts men over 50 years of age with type 2 diabetes [48]. The symptoms may develop over days/weeks and consist of pain proximally in one leg followed by muscle weakness, most pronounced in proximal muscles of the leg. The symptoms may affect both legs asymmetrically. Sensory symptoms are not as pronounced as motor symptoms, but there is usually some numbness over the anterior thigh. Recovery is slow and usually incomplete. The pathophysiological mechanism is not clear, but microvasculitis with axonal loss has been demonstrated [83].
2) Cranial neuropathies: isolated neuropathies of the extraocular nerves (n. abducens, n. trochlearis [10]). No studies have as yet shown that cranial neuropathies are more common in diabetic patients, but it is suspected that they occur with an increased frequency as compared to healthy subjects.
3) Acute painful neuropathy associated with weight loss may occur before or after the diabetes has been diag-

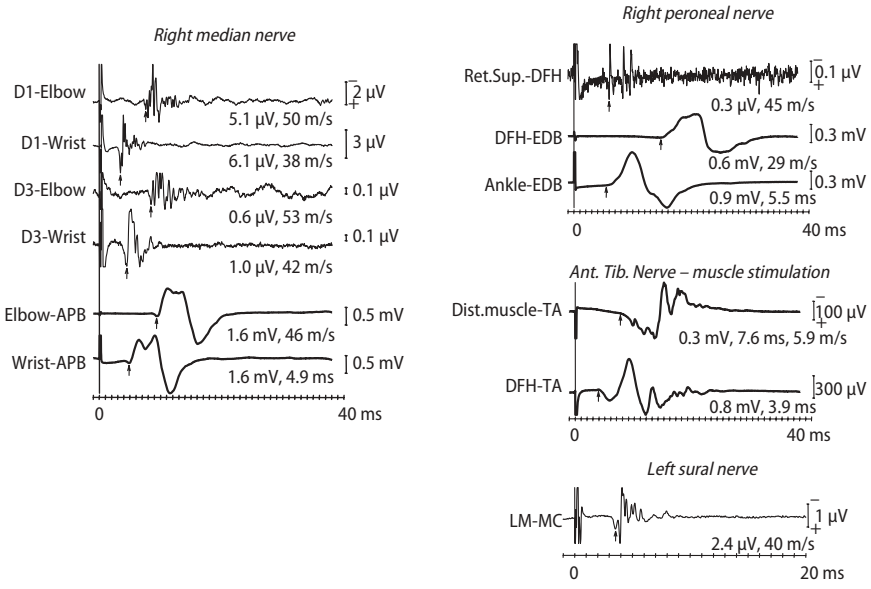

Fig. 9 Nerve conduction studies in patient described in Fig. 8. The median and peroneal nerves showed markedly reduced compound muscle action potentials (CMAP) and moderately reduced motor conduction velocities. The amplitudes of the sensory potentials (SNAP) were moderately to severely reduced in the median, peroneal and sural nerves, and the sensory conduction velocities were mildly reduced. At direct muscle stimulation of the anterior tibial muscle the amplitude of the response was reduced as was the response evoked by peroneal nerve stimulation

nosed. The main symptoms are burning feet without sensory loss or muscle weakness. Although the prognosis is favorable, recovery can take up to 10 months and may not be complete [102, 144].

Electrodiagnostic findings

The *acute painful proximal neuropathy* is axonal in type, hence EMG studies show denervation and loss of motor units in affected muscles, while sensory studies show no or only small abnormalities.

Laboratory findings

The CSF protein is normal or raised, in some instances markedly.

Uremia

Neuropathy occurs in chronic renal failure, and is usually chronic in type. The neuropathy may rarely be acute or subacute with signs of axonal loss of sensory and motor fibers. The cause of the neuropathy has not been definitely established but include speculation that it may be attributed to accumulation of "middle molecules" that are not cleared at dialysis [160]. However, recent studies of nerve fiber excitability indicate that the neuropathy may be due to raised serum potassium and associated axonal depolarization [84, 93].

Acute porphyric neuropathy

Clinical features

Acute porphyric neuropathy is usually associated with mental changes, hypertension, abdominal pain, nausea, vomiting and severe constipation. The neuropathic syndrome has an acute or subacute onset with a predominantly motor peripheral neuropathy [139]. Autonomic involvement is common in acute intermittent porphyria. Autonomic hyperactivity with persistent tachycardia may precede the onset of somatic neuropathy. The neuropathy may be precipitated by drugs such as barbiturates among others [1, 127], and usually starts symmetrically or asymmetrically in the arms followed by facial weakness and proximal weakness in the lower limbs. Tendon jerks are diminished or absent, sometimes with preserved ankle jerks. The differential diagnoses include GBS, periodic paralysis, myasthenia gravis and botulism, but porphyric neuropathy usually occurs together with mental changes and confusion and with prominent abdominal symptoms.

Electrodiagnostic findings

The neuropathy is axonal in form and mainly affects motor fibers. Motor conduction velocities are normal or slightly reduced with reduction of the CMAP, while the sensory conduction study is normal in most cases. EMG studies show denervation activity.

Laboratory findings

The porphyrin precursors δ-amino-laevulinic acid and porphobilinogen can be detected in the urine, which

may turn red/dark by exposure to sunlight. The cerebrospinal fluid may show raised protein.

Acute neuropathies induced by toxins

A number of substances and drugs are associated with peripheral neuropathies but intoxication is a rare differential diagnostic question in acute polyneuropathy. These include arsenic [63], amphiphilic cationic drugs (amiodarone and perhexiline), vincristine, cisplatin, pyridoxin, disulfiram, gold salts, glue, alcohol, and organophosphates [15, 50, 71, 154].

A severe sensory neuronopathy may occur as a complication to ingestion of amounts of *pyridoxine (vitamin B6)* that greatly exceeds the daily recommended dose of 2.5 mg [133]. The rate of onset, severity and reversibility depend on the dosage and administration of pyridoxine [16]. I. v. infusion may cause an explosive and profound neuropathy, whereas oral intake of large doses may cause a more gradual onset of symptoms. The symptoms may be reversible if the intake is discontinued early before severe degeneration has occurred though coasting effects have been described [16].

Organophosphate intoxication causes a neuropathy which develops after acute cholinergic toxicity. Treatment with *disulfiram* and *gold salts* may cause an acute, usually mild but occasionally fulminant neuropathy.

Cisplatin antineoplastic treatment is well known to cause a sensory neuronopathy dependent on the cumulative dose that may progress to profound sensory ataxia [91, 92]. The development of symptoms is usually gradual but may occur rapidly if treatment is continued beyond a limiting dose of about 300 mg/m^2.

Glue sniffing is associated with an acute or subacute sensorimotor neuropathy with autonomic features that is due to *n*-hexane (or its metabolite 2.5-hexadione). The neuropathy is associated with segmental axonal enlargements containing neurofilaments (as also seen in vincristine neuropathy, and 'giant axonal' neuropathy).

The neuropathy in *alcohol abuse* is usually insidious and chronic in type. However, in a few patients an acute proximal neuromyopathy associated with myoglobinuria may occasionally occur during bouts of heavy drinking.

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References

1. Albers JW (2001) Porphyric neuropathy. In: Mendell JR, Kissel JT, Cornblath DR (eds) Diagnosis and management of peripheral nerve disorders. Oxford University Press, Oxford, pp 344–366
2. Albers JW, Donofrio PD, McGonagle TK (1985) Sequential electrodiagnostic abnormalities in acute inflammatory demyelinating polyradiculoneuropathy. Muscle Nerve 8:528–539
3. Albers JW, Kelly JJ (1989) Acquired inflammatory demyelinating polyneuropathies: clinical and electrodiagnostic features. Muscle Nerve 12: 435–451
4. Andersen B, Westlund B, Krarup C (2003) Failure of activation of spinal motoneurones after muscle fatigue in healthy subjects studied by transcranial magnetic stimulation. J Physiol 551:345–356
5. Ang CW, Laman JD, Willison HJ, Wagner ER, Endtz HP, De Klerk MA, Tio-Gillen AP, Van Den BN, Jacobs BC, Doorn PA (2002) Structure of Campylobacter jejuni lipopolysaccharides determines antiganglioside specificity and clinical features of Guillain-Barré and Miller Fisher patients. Infect Immun 70:1202–1208
6. Antoine JC, Absi L, Honnorat J, Boulesteix JM, de Brouker T, Vial C, Butler M, De Camilli P, Michel D (1999) Antiamphiphysin antibodies are associated with various paraneoplastic neurological syndromes and tumors. Arch Neurol 56:172–177
7. Antoine JC, Honnorat J, Camdessanché JP, Magistris M, Absi L, Mosnier JF, Petiot P, Kopp N, Michel D (2001) Paraneoplastic anti-CV2 antibodies react with peripheral nerve and are associated with a mixed axonal and demyelinating peripheral neuropathy. Ann Neurol 49:214–221
8. Asbury AK (1981) Diagnostic considerations in Guillain-Barré syndrome. Ann Neurol 9(Suppl):1–5
9. Asbury AK (1987) Sensory neuronopathy. Seminars in Neurology 7:58–66
10. Asbury AK, Aldredge H, Hershberg R, Fisher CM (1970) Oculomotor palsy in diabetes mellitus: a clinico-pathological study. Brain 93:555–566
11. Asbury AK, Cornblath DR (1990) Assessment of current diagnostic criteria for Guillain-Barré syndrome. Ann Neurol 27(Suppl):S21–S24
12. Asbury AK, McKhann GM (1997) Changing views of Guillain-Barré syndrome. Ann Neurol 41:287–288
13. Asbury AK, Thomas PK (1995) The clinical approach to neuropathy. In: Asbury AK, Thomas PK (eds) Peripheral nerve disorders 2. Butterworth Heinemann, Oxford, pp 1–28
14. Behse F, Buchthal F (1978) Sensory action potentials and biopsy of the sural nerve in neuropathy. Brain 101:473–493
15. Berger AR, Schaumburg HH (2005) Human toxic neuropathy caused by industrial agents. In: Dyck PJ, Thomas PK (eds) Peripheral Neuropathy. Elsevier Saunders, Philadelphia, pp 2505–2525
16. Berger AR, Schaumburg HH, Schroeder C, Apfel S, Reynolds R (1992) Dose response, coasting, and differential fiber vulnerability in human toxic neuropathy: a prospective study of pyridoxine neurotoxicity. Neurology 42:1367–1370
17. Bolton CF (1994) Muscle weakness and difficulty in weaning from the ventilator in the critical care unit. Chest 106: 1–2
18. Bolton CF (2001) Critical illness polyneuropathy and myopathy. Crit Care Med 29:2388–2390
19. Bolton CF (2005) Neuromuscular manifestations of critical illness. Muscle Nerve 32:140–163

20. Bolton CF, Laverty DA, Brown JD, Witt NJ, Hahn AF, Sibbald WJ (1986) Critically ill polyneuropathy: electrophysiological studies and differentiation from Guillain-Barré syndrome. J Neurol Neurosurg Psychiatry 49:563–573
21. Bostock H, Cikurel K, Burke D (1998) Threshold tracking techniques in the study of human peripheral nerve. Muscle Nerve 21:137–158
22. Bradley WG, Verma A (1996) Painful vasculitic neuropathy in HIV-1 infection: Relief of pain with prednisone therapy. Neurology 47:1446–1451
23. Brown WF, Feasby TE, Hahn AF (1993) Electrophysiological changes in the acute "axonal" form of Guillain-Barré syndrome. Muscle Nerve 16:200–205
24. Buchthal F, Kamieniecka Z (1982) The diagnostic yield of quantified electromyography and quantified muscle biopsy in neuromuscular disorders. Muscle Nerve 5:265–280
25. Buchthal F, Rosenfalck P (1963) Electrophysiological aspects of myopathy with particular reference to progressive muscular dystrophy. In: Bourne GH, Golarz MN (eds) Muscular dystrophy in man and animals. S. Karger, Basel, New York, pp 193–262
26. Burke D, Kiernan MC, Bostock H (2001) Excitability of human axons. Clin Neurophysiol 112:1575–1585
27. Camdessanché JP, Antoine JC, Honnorat J, Vial C, Petiot P, Convers P, Michel D (2002) Paraneoplastic peripheral neuropathy associated with anti-Hu antibodies. A clinical and electrophysiological study of 20 patients. Brain 125:166–175
28. Chalk CH, Windebank AJ, Kimmel DW, McManis PG (1992) The distinctive clinical features of paraneoplastic sensory neuronopathy. Can J Neurol Sci 19:346–351
29. Chiba A, Kusunoki S, Obata H, Machinami R, Kanazawa I (1993) Serum anti-GQ(1b) IgG antibody is associated with ophthalmoplegia in Miller Fisher syndrome and Guillain-Barré syndrome. Clinical and immunohistochemical studies. Neurology 43: 1911–1917
30. Cornblath DR, Mcarthur JC, Kennedy PGE, Witte AS, Griffin JW (1987) Inflammatory demyelinating peripheral neuropathies associated with human T-cell lymphotropic virus Type III infection. Ann Neurol 21:32–40
31. Cornblath DR, Mendell JR, Kissel JT (2001) Evaluation of the patient with peripheral neuropathy: the challenges. In: Mendell JR, Kissel JT, Cornblath DR (eds) Diagnosis and management of peripheral nerve disorders. Oxford University Press, Oxford, pp 3–9
32. Creange A, BarlovatzMeimon G, Gherardi RK (1997) Cytokines and peripheral nerve disorders. European Cytokine Network 8:145–151
33. Creange A, Belec L, Clair B, Raphaël J-C, Gherardi RK (1996) Circulating tumor necrosis factor (TNF)-alpha and soluble TNF-alpha receptors in patients with Guillain-Barré syndrome. J Neuroimmunol 68:95–99
34. Dalakas MC, Cupler EJ (1996) Neuropathies in HIV infection. Bailliére Tindall, London, Philadelphia, Sydney, Tokyo, Toronto, pp 199–218
35. Dalmau J, Graus F, Rosenblum MK, Posner JB (1992) Anti-Hu–associated paraneoplastic encephalomyelitis/ sensory neuronopathy. A clinical study of 71 patients. Medicine (Baltimore) 71:59–72
36. Dalmau J, Gultekin HS, Posner JB (1999) Paraneoplastic neurologic syndromes: pathogenesis and physiopathology. Brain Pathol 9:275–284
37. Dalmau J, Posner JB (1996) Neurological paraneoplastic syndromes. Springer Seminars in Immunopathology 18:85–95
38. Davies L, Spies JM, Pollard JD, McLeod JG (1996) Vasculitis confined to peripheral nerves. Brain 119:1441–1448
39. de Letter MACJ, Schmitz PIM, Visser LH, Verheul FAM, Schellens RLLA, Op de Coul DAW, van der Meché FGA (2001) Risk factors for the development of polyneuropathy and myopathy in critically ill patients. Crit Care Med 29:2281–2286
40. de Letter MACJ, van Doorn PA, Savelkoul HFJ, Laman JD, Schmitz PIM, Op de Coul DAW, Visser LH, Kros JM, Teepen JLJM, van der Meché FGA (2000) Critical illness polyneuropathy and myopathy (CIPNM): evidence for local immune activation by cytokine-expression in the muscle tissue. J Neuroimmunol 106:206–213
41. de Letter MACJ, Visser LH, van der Meché FGA, Ang W, Savelkoul HFJ (2000) Distinctions between critical illness polyneuropathy and axonal Guillain-Barré syndrome. J Neurol Neurosurg Psychiatry 68:397–398
42. Delalande S, de Seze J, Fauchais AL, Hachulla E, Stojkovic T, Ferriby D, Dubucquoi S, Pruvo JP, Vermersch P, Hatron PY (2004) Neurologic manifestations in primary Sjogren syndrome: a study of 82 patients. Medicine (Baltimore) 83:280–291
43. Denny-Brown D (1948) Primary sensory neuropathy with muscular changes associated with carcinoma. J Neurol Neurosurg Psychiatry 11:73–87
44. Di Giovanni S, Mirabella M, D'Amico A, Tonali P, Servidei S (2000) Apoptotic features accompany acute quadriplegic myopathy. Neurology 55:854–858
45. Di Giovanni S, Molon A, Broccolini A, Melcon G, Mirabella M, Hoffman EP, Servidei S (2004) Constitutive activation of MAPK cascade in acute quadriplegic myopathy. Ann Neurol 55: 195–206
46. Dorfman LJ (1984) The distribution of conduction velocities (DCV) in peripheral nerves: a review. Muscle Nerve 7:2–11
47. Dorfman LJ, Cummins KL, Abraham GS (1982) Conduction velocity distributions of the human median nerve: comparison of methods. Muscle Nerve 5:S148–S153
48. Dyck PJB, Windebank AJ (2002) Diabetic and nondiabetic lumbosacral radiculoplexus neuropathies: new insights into pathophysiology and treatment. Muscle Nerve 25:477–491
49. Engel AG, Hohlfeld R (2004) The polymyositis and dermatomyositis syndromes. In: Engel AG, Franzini-Armstrong C (eds) Myology. McGraw-Hill, New York, pp 1321–1366
50. Erdem S, Kissel JT, Mendell JR (2001) Toxic neuropathies: drugs, metals, and alcohol. In: Mendell JR, Kissel JT, Cornblath DR (eds) Diagnosis and management of peripheral nerve disorders. Oxford University Press, Oxford, pp 297–343
51. Feasby TE, Gilbert JJ, Brown WF, Bolton CF, Hahn AF, Koopman WF, Zochodne DW (1986) An acute axonal form of Guillain-Barré polyneuropathy. Brain 109:1115–1126
52. Feasby TE, Hahn AF, Brown WF, Bolton CF, Gilbert JJ, Koopman WJ (1993) Severe axonal degeneration in acute Guillain-Barré syndrome: evidence of two different mechanisms? J Neurol Sci 116:185–192
53. Fisher M (1956) An unusual variant of acute idiopathic polyneuritis (syndrome of ophthalmoplegia, ataxia and areflexia). N Engl J Med 255:57–65
54. Fross RD, Daube JR (1987) Neuropathy in the Miller Fisher syndrome: Clinical and electrophysiological findings. Neurology 37:1493–1498
55. Fuller GN, Jacobs JM, Guiloff RJ (1993) Nature and Incidence of peripheral nerve syndromes in HIV infection. J Neurol Neurosurg Psychiatry 56: 372–381
56. Fuller GN, Jacobs JM, Lewis PD, Lane RJM (1992) Pseudoaxonal Guillain-Barré syndrome: severe demyelination mimicking axonopathy. A case with pupillary involvement. J Neurol Neurosurg Psychiatry 55:1079–1083

57. Garnacho-Montero J, Madrazo-Osuna J, Garcia-Garmendia JL, Ortiz-Leyba C, Jimenez-Jimenez FJ, Barrero-Almodovar A, Garnacho-Montero MC, Moyano-Del-Estad MR (2001) Critical illness polyneuropathy: risk factors and clinical consequences. A cohort study in septic patients. Intensive Care Med 27:1288–1296
58. Gastaut JL (1995) Peripheral neuropathies in HIV infection. Rev Neurol (Paris) 151:532–540
59. Gemignani F, Marbini A, Pavesi G, Divittorio S, Manganelli P, Cenacchi G, Mancia D (1994) Peripheral neuropathy associated with primary Sjögren's syndrome. J Neurol Neurosurg Psychiatry 57:983–986
60. Govoni V, Granieri E (2001) Epidemiology of the Guillain-Barré syndrome. Curr Opin Neurol 14:605–613
61. Grant IA, Hunder GG, Homburger HA, Dyck PJ (1997) Peripheral neuropathy associated with sicca complex. Neurology 48:855–862
62. Green DM, Ropper AH (2001) Mild Guillain-Barré syndrome. Arch Neurol 58:1098–1101
63. Greenberg SA (1996) Acute demyelinating polyneuropathy with arsenic ingestion. Muscle Nerve 19:1611–1613
64. Griffin JW (2001) Vasculitic neuropathies. Rheum Dis Clin North Am 27:751–60, vi
65. Griffin JW, Cornblath DR, Alexander E, Campbell J, Low PA, Bird S, Feldman EL (1990) Ataxic sensory neuropathy and dorsal root ganglionitis associated with Sjögren's syndrome. Ann Neurol 27:304–315
66. Griffin JW, Li CY, Ho TW, Xue P, Macko C, Gao CY, Yang C, Tian M, Mishu B, Cornblath DR (1995) Guillain-Barré syndrome in northern China. The spectrum of neuropathological changes in clinically defined cases. Brain 118:577–595
67. Guiloff RJ (1977) Peripheral nerve conduction in Miller Fisher syndrome. J Neurol Neurosurg Psychiatry 40: 801–807
68. Gutmann L (1999) Critical illness neuropathy and myopathy. Arch Neurol 56:527–528
69. Hartung H-P, Pollard JD, Harvey GK, Toyka KV (1995) Immunopathogenesis and treatment of the Guillain-Barré syndrome. Muscle Nerve 18:154–164
70. Hawke SH, Davies L, Pamphlett R, Guo YP, Pollard JD, McLeod JG (1991) Vasculitic neuropathy. A clinical and pathological study. Brain 114: 2175–2190
71. Herskovitz S, Schaumburg HH (2005) Neuropathy caused by drugs. In: Dyck PJ, Thomas PK (eds) Peripheral neuropathy. Elsevier Saunders, Philadelphia, pp 2553–2583
72. Ho TW, Li CY, Cornblath DR, Gao CY, Asbury AK, Griffin JW, McKhann GM (1997) Patterns of recovery in the Guillain-Barré syndromes. Neurology 48:695–700
73. Hughes RAC, Britton T, Richards M (1994) Effects of lymphoma on the peripheral nervous system. J R Soc Med 87:526–530
74. Hull RG, Morgan SH, Harding AE, Hughes GR (1984) Sjogren's syndrome presenting as a severe sensory neuropathy including involvement of the trigeminal nerve. Br J Rheumatol 23:301–303
75. Hund E (2001) Neurological complications of sepsis: critical illness polyneuropathy and myopathy. J Neurol 248:929–934
76. Hund EF (1996) Neuromuscular complications in the ICU: the spectrum of critical illness-related conditions causing muscular weakness and weaning failure. J Neurol Sci 136:10–16
77. Jacobs BC, Meulstee J, van Doorn PA, van der Meché FGA (1997) Electrodiagnostic findings related to anti-GM1 and anti-GQ1b antibodies in Guillain-Barré syndrome. Muscle Nerve 20: 446–452
78. Jacobs BC, Rothbarth PH, van der Meché FGA, Herbrink P, Schmitz PIM, deKlerk MA, van Doorn PA (1998) The spectrum of antecedent infections in Guillain-Barré syndrome: A case-control study. Neurology 51:1110–1115
79. Jamal G, Ballantyne JP (1988) The localization of the lesion in patients with acute ophthalmoplegia, ataxia and areflexia (Miller Fisher syndrome). Brain 111:95–114
80. Jamal GA, MacLeod WN (1984) Electrophysiologic studies in Miller Fisher syndrome. Neurology 34:685–688
81. Kaplan JG, Rosenberg R, Reinitz E, Buchbinder S, Schaumburg HH (1990) Invited review: peripheral neuropathy in Sjögren's syndrome. Muscle Nerve 13:570–579
82. Katsuno M, Ando T, Hakusui S, Yanagi T, Sobue G (2002) Motor conduction studies in Miller Fisher syndrome with severe tetraparesis. Muscle Nerve 25: 378–382
83. Kelkar P, Masood M, Parry GJ (2000) Distinctive pathologic findings in proximal diabetic neuropathy (diabetic amyotrophy). Neurology 55:83–88
84. Kiernan MC, Walters RJ, Andersen KV, Taube D, Murray NM, Bostock H (2002) Nerve excitability changes in chronic renal failure indicate membrane depolarization due to hyperkalaemia. Brain 125:1366–1378
85. Kissel JT, Collins MP, Mendell JR (2001) Vasculitic neuropathy. In: Mendell JR, Kissel JT, Cornblath DR (eds) Diagnosis and management of peripheral nerve disorders. Oxford University Press, Oxford, pp 202–232
86. Kissel JT, Mendell JR (1992) Vasculitic neuropathy. Neurol Clin 10:761–781
87. Krarup C (2002) Nerve conduction studies in selected peripheral nerve disorders. Curr Opin Neurol 15: 579–593
88. Krarup C (2004) Compound sensory action potential in normal and pathological human nerves. Muscle Nerve 29:465–483
89. Krarup C, Crone C (2002) Neurophysiological studies in malignant disease with particular reference to involvement of peripheral nerves. J Neurol 249:651–661
90. Krarup C, Trojaborg W (1996) Sensory pathophysiology in chronic acquired demyelinating neuropathy. Brain 119: 257–270
91. Krarup-Hansen A (1996) Cisplatin neuropati hos mus og rotter. En elektrofysiologisk og histologisk vurdering af cisplatins påvirkning af perifere nerver og dorsale rodganglier. Copenhagen University, Copenhagen, pp 1–43
92. Krarup-Hansen A, Rietz B, Krarup C, Heydorn K, Rorth M, Schmalbruch H (1999) Histology and platinum content of sensory ganglia and sural nerves in patients treated with cisplatin and carboplatin: an autopsy study. Neuropathol Appl Neurobiol 25:29–40
93. Krishnan AV, Phoon RK, Pussell BA, Charlesworth JA, Bostock H, Kiernan MC (2005) Altered motor nerve excitability in end-stage kidney disease. Brain 128:2164–2174
94. Kuwabara S, Nakata M, Sung J-Y, Mori M, Kato N, Hattori T, Koga M, Yuki N (2002) Hyperreflexia in axonal Guillain-Barré syndrome subsequent to Campylobacter jejuni enteritis. J Neurol Sci 199:89–92
95. Kuwabara S, Ogawara K, Koga M, Mori M, Hattori T, Yuki N (1999) Hyperreflexia in Guillain-Barré syndrome: relation with acute motor axonal neuropathy and anti-GM1 antibody. J Neurol Neurosurg Psychiatry 67:180–184
96. Kuwabara S, Ogawara K, Sung J-Y, Mori M, Kanai K, Hattori T, Yuki N, Lin CS, Burke D, Bostock H (2002) Differences in membrane properties of axonal and demyelinating Guillain-Barré syndromes. Ann Neurol 52: 180–187
97. Lacomis D, Zochodne DW, Bird SJ (2000) Critical illness myopathy. Muscle Nerve 23:1785–1788

98. Lange DJ, Trojaborg W, Latov N, Hays AP, Younger DS, Uncini A, Blake DM, Hirano M, Burns SM, Lovelace RE, Rowland LP (1992) Multifocal motor neuropathy with conduction block: is it a distinct clinical entity? Neurology 42:497–505
99. Leger JM, Bouche P, Bolgert F, Chaunu MP, Rosenheim M, Cathala HP, Gentilini M, Hauw JJ, Brunet P (1989) The spectrum of polyneuropathies in patients infected with HIV. J Neurol Neurosurg Psychiatry 52:1369–1374
100. Lennon VA (1994) Paraneoplastic autoantibodies: The case for a descriptive generic nomenclature. Neurology 44:2236–2240
101. Lewis RA (2005) Chronic inflammatory demyelinating polyneuropathy and other immune-mediated demyelinating neuropathies. Semin Neurol 25:217–228
102. Llewelyn JG, Tomlinson DR, Thomas PK (2005) Diabetic neuropathies. In: Dyck PJ, Thomas PK (eds) Peripheral neuropathy. Elsevier, Philadelphia, pp 1951–1991
103. Luco JV, Eyzaguirre C (1955) Fibrillation and hypersensitivity to ACh in denervated muscle: effect of length of degenerating nerve fibers. J Neurophysiol 18:65–73
104. Magistris MR, Rösler KM, Truffert A, Landis T, Hess CW (1999) A clinical study of motor evoked potentials using a triple stimulation technique. Brain 122:265–279
105. Malinow K, Yannakakis GD, Glusman SM, Edlow DW, Griffin J, Pestronk A, Powell DL, Ramsey-Goldman R, Eidelman BH, Medsger TAJ (1986) Subacute sensory neuronopathy secondary to dorsal root ganglionitis in primary Sjögren's syndrome. Ann Neurol 20:535–537
106. Manji H (2000) Neuropathy in HIV infection. Curr Opin Neurol 13: 589–592
107. McKhann GM, Cornblath DR, Griffin JW, Ho TW, Li CY, Jiang Z, Wu HS, Zhaori G, Liu Y, Jou LP (1993) Acute motor axonal neuropathy: a frequent cause of acute flaccid paralysis in China. Ann Neurol 33:333–342
108. McLeod JG (1981) Electrophysiological studies in the Guillain-Barré syndrome. Ann Neurol 9(Suppl):20–27
109. McLeod JG (1993) Paraneoplastic neuropathies. In: Dyck PJ, Thomas PK, Griffin JW, Low PA, Poduslo JF (eds) Peripheral neuropathy. WB, Saunders, Philadelphia, London, Toronto, Montreal, Sydney, Tokyo, pp 1583–1590
110. Mendell JR, Kissel JT, Cornblath DR (2001) Clues to the diagnosis of peripheral neuropathy: history and examination of the patient. In: Mendell JR, Kissel JT, Cornblath DR (eds) Diagnosis and management of peripheral nerve disorders. Oxford University Press, Oxford, pp 10–29
111. Miledi R, Slater CR (1970) On the degeneration of rat neuromuscular junctions after nerve section. J Physiol 207:507–528
112. Mori K, Iijima M, Koike H, Hattori N, Tanaka F, Watanabe H, Katsuno M, Fujita A, Aiba I, Ogata A, Saito T, Asakura K, Yoshida M, Hirayama M, Sobue G (2005) The wide spectrum of clinical manifestations in Sjogren's syndrome-associated neuropathy. Brain 128:2518–2534
113. Mori M, Kuwabara S, Fukutake T, Yuki N, Hattori T (2001) Clinical features and prognosis of Miller Fisher syndrome. Neurology 56:1104–1106
114. O'Leary CP, Willison HJ (1997) Autoimmune ataxic neuropathies (sensory ganglionopathies). Curr Opin Neurol 10:366–370
115. Oh SJ, Joy JL, Kuruoglu R (1992) "Chronic sensory demyelinating neuropathy": chronic inflammatory demyelinating polyneuropathy presenting as a pure sensory neuropathy. J Neurol Neurosurg Psychiatry 55: 677–680
116. Oh SJ, Kim DE, Kuruoglu HR (1994) What is the best diagnostic index of conduction block and temporal dispersion? Muscle Nerve 17:489–493
117. Olney RK (1999) Consensus criteria for the diagnosis of partial conduction block. Muscle Nerve 22: S225–S229
118. Padua L, Aprile I, D'Amico P, Pauri F, Sabatelli M, Caliandro P, Tonali P (2001) A useful electrophysiological test for diagnosis of minimal conduction block. Clin Neurophysiol 112: 1041–1048
119. Pardo CA, Mcarthur JC, Griffin JW (2001) HIV neuropathy: insights in the pathology of HIV peripheral nerve disease. J Peripher Nerv Syst 6:21–27
120. Park EJ, Nishida T, Sufit RL, Minieka MM (2004) Prolonged compound muscle action potential duration in critical illness myopathy. Report of nine cases. Journal of Clinical Neuromuscular Disease 5:175–183
121. Pfeiffer G, Wicklein EM, Wittig K (2000) Sensitivity and specificity of different conduction block criteria. Clin Neurophysiol 111:1388–1394
122. Plaschke M, Ohly A, Trenkwalder C, Koenig E, Lechner C (1999) Critical illness polyneuropathy in intensive care patients. Neurologic manifestation, electrophysiological investigation, and clinical outcome. Aktuelle Neurologie 26:72–80
123. Price RW (1996) Neurological complications of HIV infection. Lancet 348:445–452
124. Rich MM, Bird SJ, Raps EC, McCluskey LF, Teener JW (1997) Direct muscle stimulation in acute quadriplegic myopathy. Muscle Nerve 20: 665–673
125. Rich MM, Pinter MJ (2001) Sodium channel inactivation in an animal model of acute quadriplegic myopathy. Ann Neurol 50:26–33
126. Rich MM, Pinter MJ (2003) Crucial role of sodium channel fast inactivation in muscle fibre inexcitability in a rat model of critical illness myopathy. J Physiol 547:555–566
127. Ridley A (1984) Porphyric neuropathy. WB, Saunders, Philadelphia, pp 1704–1716
128. Said G (1998) Vasculitic neuropathies. In: Latov N, Wokke JHJ, Kelly JJ (eds) Immunological and infectious diseases of the peripheral nerves. Cambridge University Press, Cambridge, pp 158–167
129. Said G (1999) Vasculitic neuropathy. Curr Opin Neurol 12:627–629
130. Said G, Goulon-Goeau C, Lacroix C, Moulonguet A (1994) Nerve biopsy findings in different patterns of proximal diabetic neuropathy. Ann Neurol 35:559–569
131. Said G, Lacroix C, Planté-Bordeneuve V, Le Page L, Pico F, Presles O, Senant J, Remy P, Rondepierre P, Mallecourt J (2002) Nerve granulomas and vasculitis in sarcoid peripheral neuropathy: a clinicopathological study of 11 patients. Brain 125:264–275
132. Saperstein DS, Amato AA, Wolfe GI, Katz JS, Nations SP, Jackson CE, Bryan WW, Burns DK, Barohn RJ (1999) Multifocal acquired demyelinating sensory and motor neuropathy: the Lewis-Sumner syndrome. Muscle Nerve 22:560–566
133. Schaumburg H, Kaplan J, Windebank A, Vick N, Rasmus S, Pleasure D, Brown MJ (1983) Sensory neuropathy from pyridoxine abuse. A new megavitamine syndrome. N Engl J Med 309:445–448
134. Schwarz J, Planck J, Briegel J, Straube A (1997) Single-fiber electromyography, nerve conduction studies, and conventional electromyography in patients with critical-illness polyneuropathy: evidence for a lesion of terminal motor axons. Muscle Nerve 20:696–701

135. Sghirlanzoni A, Pareyson D, Lauria G (2005) Sensory neuron diseases. Lancet Neurol 4:349–361
136. Shimamura H, Miura H, Iwaki Y, Kubodera T, Matsuoka T, Yuki N, Koga M (2002) Clinical, electrophysiological, and serological overlap between Miller Fisher syndrome and acute sensory ataxic neuropathy. Acta Neurol Scand 105:411–413
137. Smith KJ, Hall SM (2001) Factors directly affecting impulse transmission in inflammatory demyelinating disease: recent advances in our understanding. Curr Opin Neurol 14:289–298
138. Stefurak TL, Midroni G, Bilbao JM (1999) Vasculitic polyradiculopathy in systemic lupus erythematosus. J Neurol Neurosurg Psychiatry 66: 658–661
139. Suarez JI, Cohen ML, Larkin J, Kernich CA, Hricik DE, Daroff RB (1997) Acute intermittent porphyria: clinicopathologic correlation. Report of a case and review of the literature. Neurology 48:1678–1683
140. Susuki K, Nishimoto Y, Yamada M, Baba M, Ueda S, Hirata K, Yuki N (2003) Acute motor axonal neuropathy rabbit model: immune attack on nerve root axons. Ann Neurol 54: 383–388
141. Susuki K, Odaka M, Mori M, Hirata K, Yuki N (2004) Acute motor axonal neuropathy after Mycoplasma infection: Evidence of molecular mimicry. Neurology 62:949–956
142. Takada H, Ravnborg M (2000) Magnetically evoked motor potentials in demyelinating and axonal polyneuropathy: a comparative study. Eur J Neurol 7:63–69
143. Tankisi H, Pugdahl K, Fuglsang-Frederiksen A, Johnsen B, de CM, Fawcett PR, Labarre-Vila A, Liguori R, Nix WA, Schofield IS (2005) Pathophysiology inferred from electrodiagnostic nerve tests and classification of polyneuropathies. Suggested guidelines. Clin Neurophysiol 116: 1571–1580
144. Thomas PK (1997) Clinical features and investigation of diabetic somatic peripheral neuropathy. Clin Neurosci 4:341–345
145. Thomas PK, Ochoa J (1993) Clinical features and differential diagnosis. In: Dyck PJ, Thomas PK, Griffin JW, Low PA, Poduslo JF (eds) Peripheral Neuropathy. WB, Saunders, Philadelphia, London, Toronto, Montreal, Sydney, Tokyo, pp 749–774
146. Trojaborg W (1990) Quantitative electromyography in polymyositis: a reappraisal. Muscle Nerve 13:964–971
147. Trojaborg W, Weimer LH, Hays AP (2001) Electrophysiologic studies in critical illness associated weakness: myopathy or neuropathy – a reappraisal. Clin Neurophysiol 112: 1586–1593
148. van Mook WN, Hulsewe-Evers RP (2002) Critical illness polyneuropathy. Curr Opin Crit Care 8:302–310
149. Vilppula A (1972) Muscular disorders in some collagen diseases. A clinical, electromyographic and biopsy study. Acta Medica Scandinavica Suppl 540: 7–47
150. Vucic S, Cairns KD, Black KR, Tick Chong PS, Cros D (2004) Neurophysiologic findings in early acute inflammatory demyelinating polyradiculoneuropathy. Clin Neurophysiol 115: 2329–2335
151. Willison HJ (2001) Fine specificity of anti-GQ1b antibodies and clinical features. J Neurol Sci 185:1–2
152. Willison HJ, O'Hanlon GM (1999) The immunopathogenesis of Miller Fisher syndrome. J Neuroimmunol 100:3–12
153. Wilmshurst P (1996) Critical illness polyneuropathy. Lancet 348:414
154. Windebank AJ (2005) Metal neuropathy. In: Dyck PJ, Thomas PK (eds) Peripheral neuropathy. Elsevier Saunders, Philadelphia, pp 2527–2551
155. Winkelman C (2004) Inactivity and inflammation: selected cytokines as biologic mediators in muscle dysfunction during critical illness. AACN Clin Issues 15:74–82
156. Woittiez AJ, Veneman TF, Rakic S (2001) Critical illness polyneuropathy in patients with systemic inflammatory response syndrome or septic shock. Intensive Care Med 27:613
157. Yuki N, Kuwabara S, Koga M, Hirata K (1999) Acute motor axonal neuropathy and acute motor-sensory axonal neuropathy share a common immunological profile. J Neurol Sci 168:121–126
158. Yuki N, Yamada M, Koga M, Odaka M, Susuki K, Tagawa Y, Ueda S, Kasama T, Ohnishi A, Hayashi S, Takahashi H, Kamijo M, Hirata K (2001) Animal model of axonal Guillain-Barré syndrome induced by sensitization with GM1 ganglioside. Ann Neurol 49: 712–720
159. Zifko UA, Zipko HT, Bolton CF (1998) Clinical and electrophysiological findings in critical illness polyneuropathy. J Neurol Sci 159:186–193
160. Zochodne DW (2005) Neuropathies associated with renal failure, hepatic disorders, chronic respiratory disease, and critical disease. In: Dyck PJ, Thomas PK (eds) Peripheral neuropathy. Elsevier Saunders, Philadelphia, pp 2017–2037