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Guidelines

# Current status on electrodiagnostic standards and guidelines in neuromuscular disorders

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ABSTRACT

The aim of this review is to present the status of electrodiagnostic standards and guidelines in neuromuscular disorders. Electrodiagnostic guidelines are developed on the background of medical technology assessment, wherefore a short presentation of medical technology assessment is given covering: (1) Evidence-based medicine, i.e. "to do the right thing", describing practice parameters and the STARD initiative which introduces evidence-based medicine in electrodiagnostic medicine, (2) Continuous quality improvement, i.e. "to do the thing right", describing variation among laboratories in methods and interpretation of tests, and the need for medical audit and implementation of electrodiagnostic guidelines, (3) Outcome studies, i.e. "is it worthwhile to do the right thing right?". In electrodiagnostic medicine there are very few outcome studies.

Standards and guidelines described in the literature for different neuromuscular disorders are presented, often as figures or tables. These cover guidelines developed in detail for CIDP by expert consensus multicentre groups by AAN, INCAT, EFNS/PNS and for other inflammatory demyelinating neuropathies are described, as well as guidelines differentiating between demyelinating pathophysiology and axonal loss by motor and sensory nerve conduction studies.

Furthermore, electrodiagnostic guidelines for ALS as detailed in the El Escorial, the modified El Escorial and the recent supplementary Awaji criteria are described and presented in a comprehensive table. Only few electrodiagnostic guidelines are published for nerve entrapment, cervical radiculopathy and neuromuscular transmission failure whereas none are known for myopathy. If no electrodiagnostic criteria for a given disorder exist, criteria for the electrodiagnostic examination are described if present.

It is concluded that future research is needed in order to develop more electrodiagnostic guidelines in neuromuscular disorders by international expert consensus groups. Such research should use an evidence-based medicine approach and medical technology assessment and include continuous quality development and outcome studies.


**Contents**



*Abbreviations:* MAP, compound muscle action potential; CB, conduction block; CTS, carpal tunnel syndrome; CV, conduction velocity; DML, distal motor latency; LN, lower limit of normal; LMN, lower motor neuron; NCS, nerve conduction studies; PNP, polyneuropathy; SD, standard deviation; SNAP, sensory nerve action potential; TD, temporal dispersion; UE, upper extremities; ULN, upper limit of normal; UMN, upper motor neuron.

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## 1. Introduction

Clinical standards and guidelines, or practice parameters, are increasingly obtaining more focus in the health care system. This is partly a consequence of the increasing financial pressure on the health system and the rapid introduction of new technology, which makes it increasingly important to seek evidence to justify the use of any particular form of medical practice, regarding both examination and treatment (Kitchener, 2002). In addition, marked variation in practice patterns can also lead to concern about differences in the quality of patient care (Cohen et al., 1996; Lomas et al., 1989). Dissemination of standards and guidelines for neurophysiological examination and diagnosis of neuromuscular disorders will give a more precise prognosis and optimal treatment of the individual patient, and improve the selection of patients for research studies.

This review aims at providing a status of the current clinical standards and guidelines within electrodiagnostic medicine and to give a short introduction to the principles behind their development. The references are selected by the authors and the selection may thus be biased. This is in contrast to a guideline development where an expert group goes through all relevant literature using systematic search via Internet search machines such as Medline and Embase. Often such an evidence-based guideline consists of a great amount of material which may take up a full monograph and is outside the scope of this review.

## 2. Medical technology assessment

Optimal standards and guidelines should be built on medical technology assessment, which can be divided into three parts:

- Evidence-based medicine; i.e. "*to do the right thing*". This includes practice parameters and improved quality of the reporting of studies of diagnostic accuracy as suggested in the STARD initiative (Bossuyt et al., 2003).
- Continuous quality improvement. i.e. "*to do the right thing right*", including studies of variation in electrodiagnostic medicine and medical audit.
- Outcome studies and cost-benefit analysis, i.e. "*is it worthwhile to do the right thing right?*". There are very few outcome studies in electrodiagnostic medicine examining whether the patients have benefitted from the neurophysiological examination with respect to diagnosis or treatment, and whether there is an economical effect for society.

In the following, the basic ideas and relevant neurophysiological studies for each point are outlined in short.

### 2.1. Evidence-based medicine

There are numerous studies on sensitivity and specificity of electrodiagnostic methods applied on patients with neuromuscular disorders and reference populations (controls) (Fuglsang-Frederiksen, 2006). However, only a few of these studies score more than class IV for evidence support, as they lack blinding, a reference standard (gold standard), or a prospective design as suggested by the American Association of Electrodiagnostic Medicine (AAEM) (Table 1) (Dubinsky et al., 2003; Marciniak et al., 2005).

In general, evidence-based documentation within diagnostic methods is much less than within therapeutic trials. One of the reasons for this difference is, that a blinded prospective study using a reference standard and optimal random selection of patients is very resource-demanding, and resources are less in diagnostic dis-

**Table 1**
Practice recommendations based on evidence level of diagnostic studies (Dubinsky et al., 2003; Knopman et al., 2001).

| Class | |
|---|---|
| I | Evidence provided by a well-designed prospective study in broad spectrum of persons with the suspected condition, using a "gold standard" for case definition, in which test is applied in a blinded evaluation, and enabling the assessment of appropriate tests of diagnostic accuracy |
| II | Evidence provided by a well-designed prospective study of a narrow spectrum of persons with the suspected condition, or a well-designed retrospective study of a broad spectrum of persons with an established condition (by "gold standard") compared with a broad spectrum of controls, in which test is applied in blinded evaluation, and enabling the assessment of appropriate tests of diagnostic accuracy |
| III | Evidence provided by a retrospective study in which either persons with the established condition or controls are of a narrow spectrum, and in which test is applied in a blinded evaluation |
| IV | Any design in which test is not applied in blinded evaluation OR evidence provided by expert opinion alone or in descriptive case series (without controls) |
| *Recommendation* | |
| Standard | Principle for patient management that reflects a high degree of clinical certainty (usually this requires Class I evidence that directly addresses the clinical question, or overwhelming Class II evidence when circumstances preclude randomized clinical trials) |
| Guideline | Recommendation for patient management that reflects moderate clinical certainty (usually this requires Class II evidence or a strong consensus of Class III evidence) |
| Practice option | Strategy for patient management for which the clinical utility is uncertain (inconclusive or conflicting evidence or opinion) |
| Practice advisory | Practice recommendation for emerging and/or newly approved therapies or technologies based on evidence from at least one Class I study. The evidence may demonstrate only a modest statistical effect or limited (partial) clinical response, or significant cost–benefit questions may exist. Substantial (or potential) disagreement among practitioners or between payers and practitioners may exist |

ciplines than in treatment-driven research. Nevertheless, our patients with neuromuscular disorders would much benefit from evidence-based diagnostic studies.

#### 2.1.1. Practice parameters for electrodiagnostic medicine

The American Association for Neuromuscular and Electrodiagnostic Medicine (AANEM), previously AAEM has done a huge effort on development and dissemination of practice parameters by publishing several papers with recommendations for electrodiagnostic medicine. These include examination protocols and/or diagnostic criteria for the most frequent neurophysiological diagnoses (AAEM, 1999a,b, 2002; AAEM and Campbell, 1999; AAEM Quality Assurance Committee, 2001; England et al., 2005, 2009; Jablecki et al., 2002; Marciniak et al., 2005; Olney et al., 2003; Patel et al., 2005).

These recommendations are developed by consensus groups and build on literature search followed by review of articles and selection of relevant articles. The articles are graded after evidence-based quality by grades from Class I with lowest risk of bias (e.g. a prospective randomised controlled blinded study) to grade of Class IV with highest risk of bias (e.g. expert opinion), and the strength of the recommendation graded from 'Standard' with the highest level of scientific evidence to 'Practice Advisory', where only limited scientific evidence is present (Table 1) (Dubinsky et al., 2003; Knopman et al., 2001).

#### 2.1.2. STARD initiative

Evidence-based documentation for an electrodiagnostic method can be obtained using STARD (STAndards for the Reporting of Diagnostic accuracy studies), an initiative aiming at "improving the accuracy and completeness of reporting of studies of diagnostic accuracy to allow readers to assess the potential for bias in the study (internal validity) and to evaluate its generalisability (external validity)" (Bossuyt et al., 2003). The STARD statement includes 25 checkpoints and was published in 12 major journals. The 25 checkpoints mostly concern methods and results and include selection of subjects, reference standard, prospective versus retrospective, blinded (masked) or not, statistical methods, test reproducibility, diagnostic accuracy and measures of statistical uncertainty. Although the quality of reporting has improved only slightly since the publication of the STARD statement (Smidt et al., 2006), the authors of this review stress the importance of introducing the STARD statement in clinical neurophysiology and its journals.

### 2.2. Continuous quality improvement

The first step in quality development is identification of the quality problem. Studies of variation within a given field is a useful tool for recognising a quality problem by identifying areas with a potential need for further development and improvements, as variation may result from differences in education, culture or reimbursement policies, but may also indicate that the scientific grounding for decisions is uncertain (Johnsen et al., 1995). Wide variation in medical practices is well documented in several medical disciplines and seems to be the rule rather than the exception (James and Hammond, 2000; Palmer and Lawthers, 1991; Westert and Groenewegen, 1999). At worst, variation in clinical practice, together with medical uncertainty and even lack of knowledge, may not only contribute to misapplication of resources and available services but in particular may lead to questionable results for the patients (Veloso et al., 1995).

The identification of a problematic area should be followed by a medical audit, which is defined as "a systematic critical analysis of the quality of medical care, including the procedures used for diagnosis and treatment, the use of resources, and the resulting outcome for the patient" (NHS working for patients, 1989). Medical audit includes a set up of criteria and standards and collection of relevant data, or indicators, to perform quality assessment. The quality level can then be evaluated and in case of non-satisfying results, the problem should be identified and the process repeated (Mainz, 2003). Peer review medical audit has been widely accepted as suitable for quality improvement in medical practice, because it encourages professional autonomy and supports critical insight and appraisal of quality of care (Beyer et al., 2003). Peer review groups may be described as small groups of physicians, based on voluntary participation and concerned with activities aimed at assessing and continuously improving the quality of patient care (e.g. by audit, guideline setting or adaptation, critically discussing personal medical practice, making plans for change).

#### 2.2.1. Reference data and limits of normal

An ideal reference data set is sampled and analysed in your own laboratory. However, sampling and analysing of reference data are time-consuming and in practice may take years (Rosenfalck and Rosenfalck, 1975). Alternatively, reference data sampled in a laboratory where you have been trained in the specific method can be used. A third possibility is to sample reference data in multicentre projects, however, even with the same protocol differences between laboratories may be seen (Johnsen et al., 2006). The way

to use reference data varies from laboratory to laboratory and from neurophysiology school to neurophysiology school, especially concerning the limit of normal, with the most frequently used being: (a) percentage deviation from mean or median of controls, (b) percent deviation from or of the upper or lower limit of normal (ULN/LLN), or (c) specific percentiles or normal deviation (Dyck et al., 2001) or (d) in our laboratory we use mean ± 2 standard deviations (SD) as limit for controls, i.e. approx. corresponding to the 95% confidence limit, and state the deviation from normal mean for the individual subject as *Z*-scores, i.e. deviations in SD from the normal of mean (Tankisi et al., 2005). This requires that the reference data is normally distributed; sometimes it is necessary to use a logarithmic transformation to obtain this, e.g. for some action potential amplitude data. The advantages of using *Z*-score are that this is comparable among subjects even when correction is needed, for instance between different nerves and extremities, and regarding male/female, age and height (Campbell and Robinson, 1993; Fuglsang-Frederiksen et al., 1989; Jabre and Sato, 1990).

### 2.2.2. Variation studies in clinical neurophysiology

The electrodiagnostic examination of patients with neuromuscular disorders is prone to show a great deal of variation as a series of diagnostic tests is applied to a clinical problem, with the performance and selection of tests being highly operator dependent.

Variation among clinical neurophysiologists was at first documented in an evaluation of the EMG decision support system KANDID (Fuglsang-Frederiksen et al., 1989) showing differences in diagnostic agreement with KANDID in 10–20% of the patient cases and a pronounced inter-examiner variation in the agreement level among physicians from different EMG centres. The disagreement was interpreted as due to differences in epidemiology, examination technique, reference data and examination planning strategies including diagnostic criteria (Vingtoft et al., 1993).

Studies in ESTEEM (European Standardised Telematic tool to Evaluate Electrodiagnostic Methods), an ongoing multicentre project initiated in 1992 with the aim of raising the quality of electrodiagnostic examinations in Europe (Veloso et al., 1995; Vingtoft et al., 1995), have revealed great variation among European electrodiagnostic laboratories regarding referral pattern and distribution of diagnoses (Johnsen et al., 1994), in the performance of the electrophysiological examination regarding techniques, number of performed and abnormal tests per patient, and in pathophysiological interpretation of electrophysiological tests in mixed groups of patients (Fuglsang-Frederiksen et al., 1995, 1999; Johnsen et al., 1995) and in patients with polyneuropathy (Finnerup et al., 1998; Johnsen et al., 1995; Pugdahl et al., 2005; Tankisi et al., 2003, 2006) and ALS (Pugdahl et al., in press).

Besides from the studies done in the ESTEEM project, there have only been few studies specifically investigating variation in electrodiagnostic practice. Two studies examined intra- and inter-examiner reliability on the performance of nerve conduction studies (NCS) in normal subjects (Chaudhry et al., 1991) and in patients with mild diabetic polyneuropathy (Chaudhry et al., 1994), and a large multicentre study among 60 centres demonstrated a low test–retest variability when a common protocol was followed (Bril et al., 1998). A fair interrater reliability of EMG recordings in lumbosacral radiculopathy among experienced electromyographers have been reported, however, the interrater reliability among less experienced examiners was poor (Kendall and Werner, 2006).

*Comments:* The variation described here suggests that introducing more standards and well-defined criteria or guidelines for the electrophysiological examination of neuromuscular disorders may improve the quality of the examination. Importantly, introduction and discussion of standards, criteria and guidelines should be firmly integrated into training programmes for new neurophysiologists.

### 2.2.3. Two extreme practices

Two main approaches to the neurophysiological examination have been identified (Fuglsang-Frederiksen et al., 1995). In one approach, the selection of tests are guided by the clinical presentation and adjusted according to the results of the other tests as the examination proceeds. Another approach for reaching an EMG diagnosis is to apply an often long series of different diagnostic tests, which individually reveals something about the electrophysiological condition in different test structures, and then combine the mosaic of diagnostic information from each of these tests into a diagnosis, i.e. a form of an electrodiagnostic screening.

*Comments:* We recommend that EMG studies should be guided by the clinical findings and interpreted in relation to the full clinical picture. Electrodiagnostic screening without clinical correlation of the results may lead to false positive or negative results for specific conditions (Robinson et al., 1998, 2000), which may result in either unnecessary surgeries and medical therapies or delay of treatment, respectively.

### 2.2.4. Medical audit in clinical neurophysiology

Peer review medical audit in the ESTEEM project have most likely introduced changes towards a more uniform practice among the physicians in terms of examination techniques, number of examined nerve segments, interpretation of NCS and classification of polyneuropathy (Finnerup et al., 1998; Tankisi et al., 2006; Pugdahl et al., 2005). Although most changes have been minor it was concluded that it seems possible to change the EMG practice of individual physicians by peer review medical audit. However, although repetitive peer reviews and consensus meetings may increase the quality of examinations performed by the members of such groups and perhaps the colleagues in laboratories concerned, a more widespread increase in quality by these methods is not possible. For a larger scale dissemination of evidence-based research results or consensus recommendations published guidelines and standards are required.

**Table 2**
Utility of electrodiagnostic studies.

| | *Diagnosis after electrodiagnostic examination* | | | *Study design* | | |
|---|---|---|---|---|---|---|
| | Altered (%) | Confirmed (%) | Not clarified (%) | No. of patients | Prospective/follow-up | Referral disorder |
| Kothari et al. (1995) | 39 | 60 | 0 | 126 (76)[a] | −/− | Consecutive mixed |
| Kothari et al. (1998) | 37 | 63 | 0 | 140 (78)[a] | +/+ (100) | Consecutive mixed |
| Haig et al. (1999) | 42 | 37 | 21 | 255 | +/− | UE complaints |
| Nardin et al. (2002) | 31 | 58 | 9 | 100 (79)[b] | +/ + | Weakness |
| Cho et al. (2004) | 43 | 39 | 18 | 590 | −/− | Distal parasthesia, PNP |
| Cocito et al. (2006) | 60 | 40 | 0 | 3900 | −/− | Consecutive mixed |
| Perry et al. (2009) | 13 (27)[c] | 53 | 17 | 98 | −/− | Consecutive inpatients |

[a] Number of patients with abnormal findings.
[b] Number of patients with a final diagnosis at follow-up.
[c] Diagnostic evaluation, treatment, or both changed.

### 2.3. Outcome studies

Outcome studies in electrodiagnostic medicine in patients with neuromuscular disorders are very sparse. A handful of differently designed studies most often on mixed patient groups has looked at the diagnosis reached after the electrodiagnostic study in comparison to the referral diagnosis or referral symptoms (Cho et al., 2004; Cocito et al., 2006; Haig et al., 1999; Kothari et al., 1995, 1998; Nardin et al., 2002; Perry et al., 2009). The percentage of patients in whom the diagnosis had been altered as a consequence of the electrodiagnostic examination ranged from 13% to 60% in the different studies (Table 2) (So, 2009).

#### 2.3.1. Evaluations of the impact of guidelines

In a prospective multicenter study the implementation of restrictive diagnostic guidelines for chronic polyneuropathies improved cost efficiency by reducing the number of routine laboratory tests required per patient by 27% despite low guideline adherence (Vrancken et al., 2006). In contrast, other studies showed that app. 1/3 of patients who underwent carpal tunnel release may have had an inadequate electrodiagnostic study according to the AAEM practice guidelines before the surgery (Storm et al., 2005), and that 50% of patients who had clinically typical MMN but were not fulfilling the AAEM criteria for definite or probable conduction block responded to IVIg treatment (Nobile-Orazio et al., 2002).

## 3. Guidelines

Standards and guidelines for the electrodiagnostic examination of a certain disorder should cover *examination strategy* i.e. techniques and number of tests to perform, as well as *diagnostic strategy or minimal criteria*, i.e. degree of abnormality and number of abnormal anatomical structures required for accepting the diagnosis. The examination strategy is more variable and depends on the type of test used, i.e. quantitative or qualitative tests, needle or surface recordings, whereas minimal criteria for accepting a diagnosis are more independent of techniques.

Neurophysiological criteria can be established both at the *nerve or muscle level*, e.g. degree of conduction slowing indicating demyelination in a nerve, as well as the *patient level*, i.e. number and distribution of abnormal studies required for diagnosing or classifying a given disorder (Fuglsang-Frederiksen et al., 1995; Johnsen et al., 1995; Tankisi et al., 2005).

The following sections review the existing electrodiagnostic criteria on different neuromuscular disorders, mostly suggested by consensus expert groups. In addition some examination practice parameters are described. Standards for instrumentation of EMG

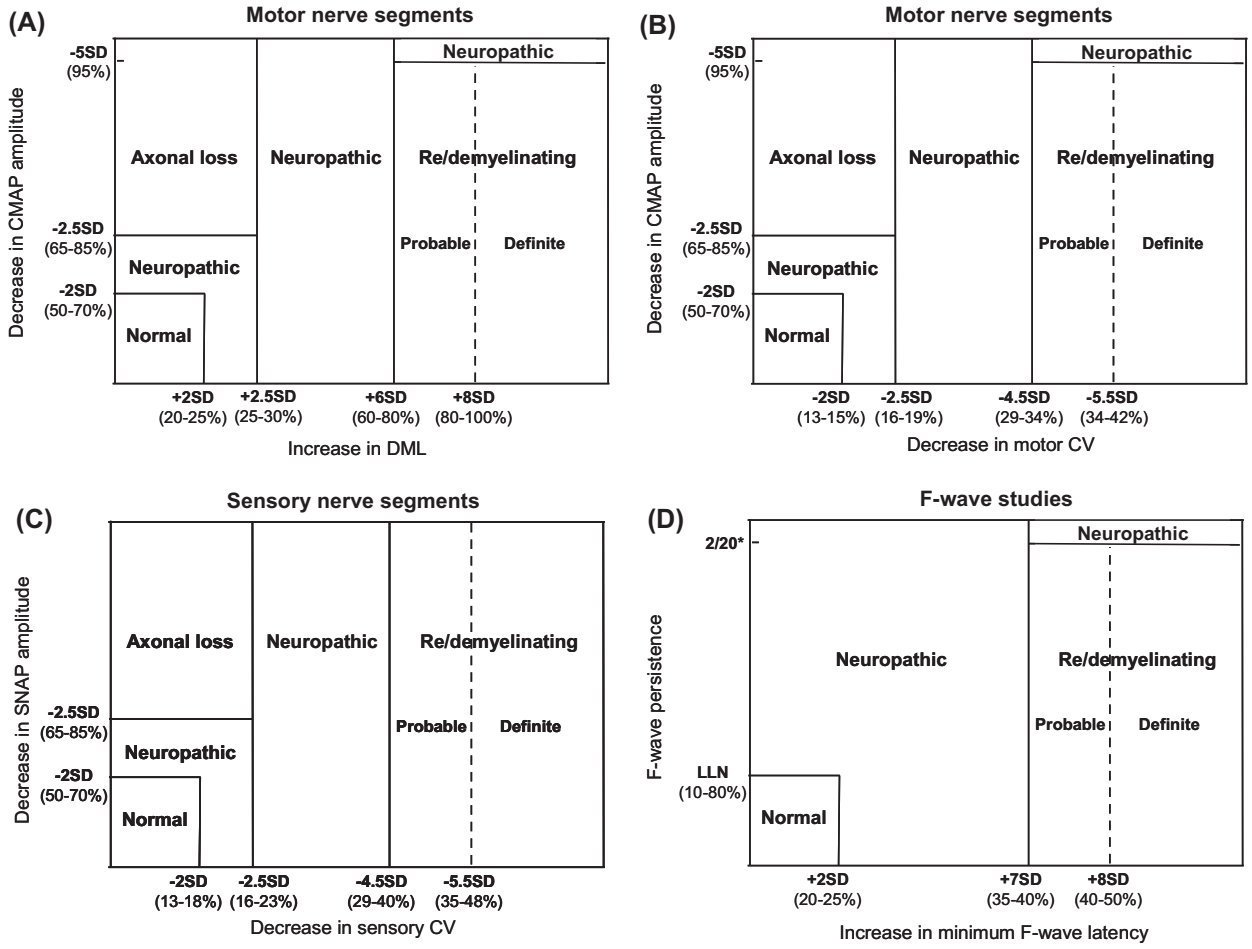


**Fig. 1.** Diagrams for pathophysiological interpretation of nerve conduction studies suggested by the ESTEEM group. (A–C) Motor and sensory nerve segments are classified as demyelinating, axonal or neuropathic according to the degree of conduction slowing (*x*-axis) and amplitude decrease (*y*-axis). The term neuropathic is used to indicate a grey zone where a clear electrodiagnostic distinction between demyelinating and axonal pathophysiologies cannot be made. The suggested limits are presented in SD from mean of controls, i.e. *Z*-scores, with the corresponding percentages in parentheses. (D) Similarly F-wave studies are classified as demyelinating or neuropathic based the F-wave latency *Z*-score and the F-wave persistence compared to LLN. *To infer demyelination recording of at least 2 F-waves/20 stimuli is required. Reprinted from Tankisi et al. (2005) with permission from Elsevier.

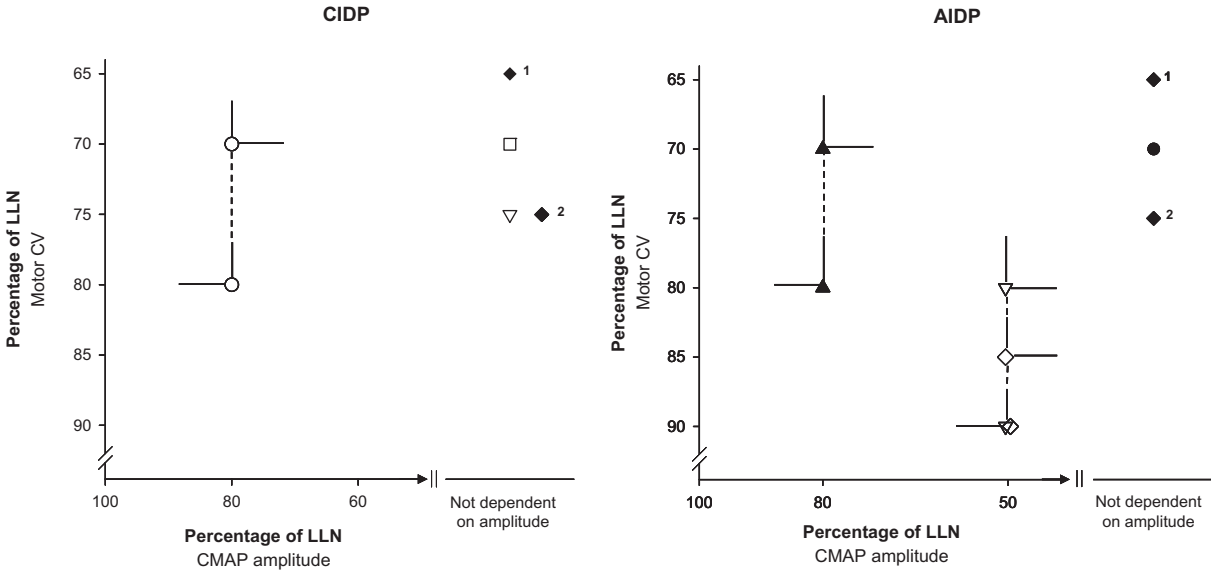


**Fig. 2.** Demyelination criteria for motor CV in relation to CMAP amplitude in CIDP and AIDP. The required decrease in CV (*y*-axis) according to a given reduction in CMAP amplitude (*x*-axis) is indicated. Symbols: ○ AAN (1991), Hughes et al. (2001), Saperstein et al. (2001), Nicolas et al. (2002), Thaisetthawatkul et al. (2002), Koski et al. (2009); ▽ Albers and Kelly (1989); □ Barohn et al. (1989), Van den Bergh and Pieret (2004), Joint task force of the EFNS and the PNS (2010); ▲ Asbury and Cornblath (1990), Italian GBS study group (1996); ◇ Ho et al., (1995), Hadden et al. (1998); ● Meulstee and van der Meche (1995), Van der Meché et al. (2001); ♦ Tankisi et al., 2005 (1: probable, 2: definite).

(Bischoff et al., 1999), motor NCS (Falck and Stalberg, 1995), and sensory NCS with needle (Trojaborg, 1992) or surface recording (Falck et al., 1994) are on the other hand quite well accepted and are not further described.

The majority of existing standards and guidelines concern the examination and diagnosis of polyneuropathy, especially chronic inflammatory demyelinating polyradiculopathy (CIDP), whereas guidelines for most other conditions in general are sparse. Clinical diagnostic criteria for different kinds of polyneuropathy are not described in detail in this review focused on electrodiagnostic criteria.

### 3.1. Polyneuropathy

The neurophysiological examination provides invaluable information for the diagnosis, prognosis and treatment of polyneuropathy. The classification of a polyneuropathy with regard to demyelination or axonal degeneration constitutes the major challenge of the examination.

At the electrophysiological level there is a huge amount of literature on criteria for demyelination, but only little on axonal loss. In the interpretation of a NCS one should be aware of a grey zone, i.e. an area where a nerve abnormality is proven but a distinction

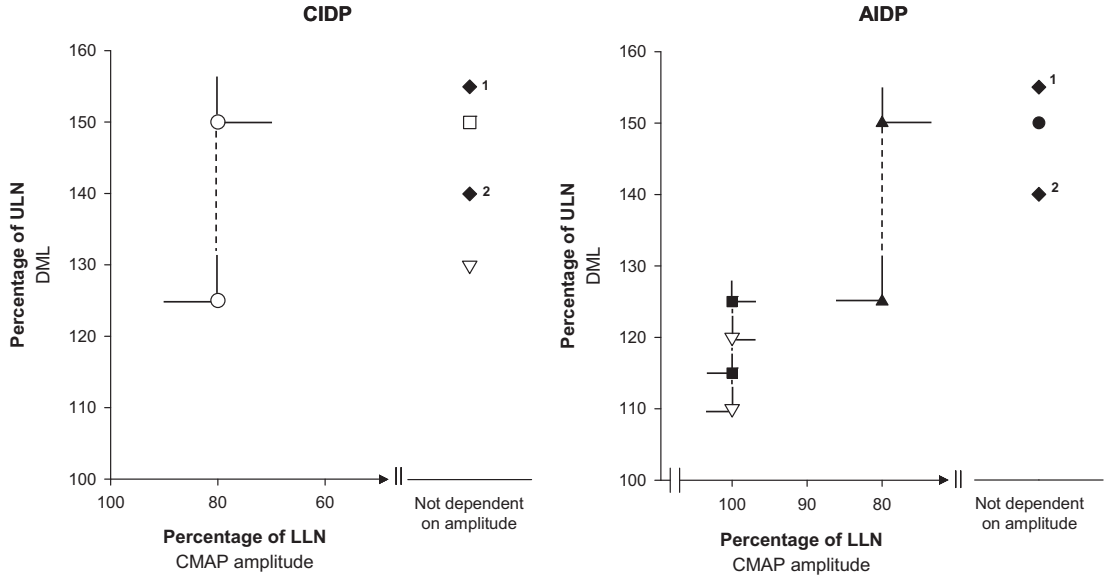


**Fig. 3.** Demyelination criteria for DML in relation in relation to CMAP amplitude. The required increase in DML (*y*-axis) according to a given reduction in CMAP amplitude (*x*-axis) is indicated. Symbols: ○ AAN (1991), Hughes et al. (2001), Saperstein et al. (2001), Nicolas et al. (2002), Thaisetthawatkul et al. (2002), Koski et al. (2009); ▽ Albers and Kelly (1989); □ Van den Bergh and Pieret (2004), Joint task force of the EFNS-PNS Task Force (2010); ■ Ho et al. (1995), Hadden et al. (1998); ▲ Asbury and Cornblath (1990), Italian GBS study group (1996); ● Meulstee and van der Meche (1995), Van der Meché et al. (2001); ♦ Tankisi et al. (2005) (1: probable, 2: definite).

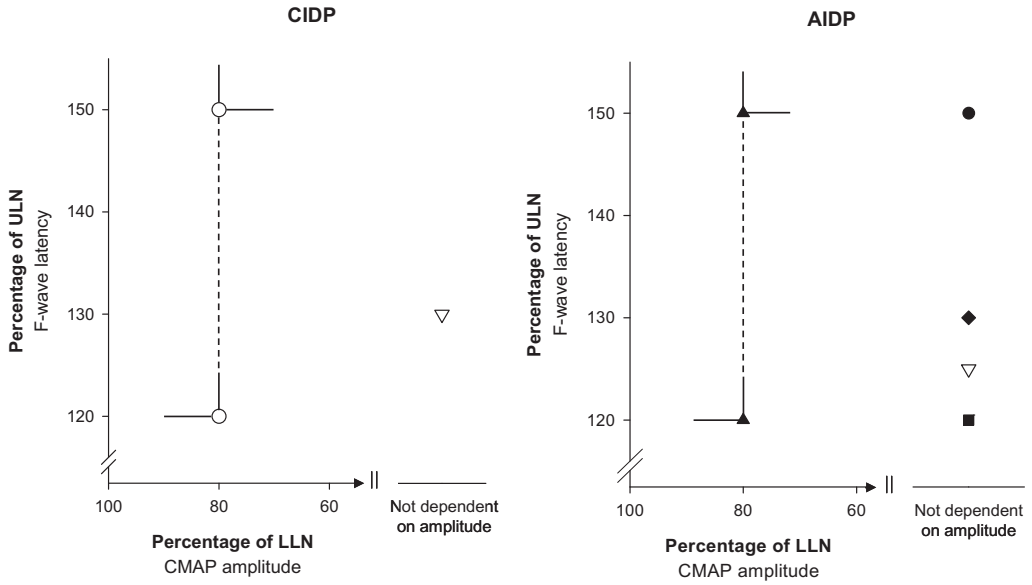


**Fig. 4.** Demyelination criteria for F-wave minimum latency in relation to CMAP amplitude in CIDP and AIDP. The required increase in F-wave latency (*y*-axis) according to a given reduction in CMAP amplitude (*x*-axis) is indicated. Symbols: ○ AAN (1991), Hughes et al. (2001), Saperstein et al. (2001), Nicolas et al. (2002), Thaisetthawatkul et al. (2002), Van den Bergh and Pieret (2004), Joint task force of the EFNS and the PNS (2010), Koski et al. (2009), ▽ Albers and Kelly (1989); ▲ Asbury and Cornblath (1990), Italian GBS study group (1996); ■ Ho et al. (1995), Hadden et al. (1998); ● Meulstee and van der Meche (1995), Van der Meché et al. (2001); ♦ Tankisi et al. (2005).

between demyelination and axonal loss can not be made either due to the nature of the pathophysiological process or to problems inherited in the electrodiagnostic method. This was evidenced in studies of patients with peroneal muscular atrophy classified by biopsy, where an overlap in motor CV or DML in some cases were seen between the axonal and demyelinating types (Bouche et al., 1983; Buchthal and Behse, 1977). The main reason for the difficulty in discriminating primary demyelination from primary axonal loss is that conduction slowing, in addition to involvement of myelin or Schwann cells in demyelinating neuropathy, can also be caused by secondary loss of fast conducting, large-diameter fibres in axonal neuropathy. Similarly, CMAP or SNAP amplitude reduction can in addition to axonal degeneration and loss of fibres in axonal neuropathy also be due to temporal dispersion or secondary axonal degeneration in demyelinating neuropathy (Johnsen and Fuglsang-Frederiksen, 2000; Tankisi et al., 2007). In fact, in contrast to what would be expected, the amplitudes are often more decreased in demyelinating than in axonal polyneuropathies (Buchthal and Behse, 1977; Harding and Thomas, 1980; Tankisi et al., 2007). Several guideline criteria operate with two different limits for conduction slowing requiring a greater decrease in CV or increase in distal motor latency (DML) and F-wave latency if the amplitude is decreased below a certain level, typically to 80% or 50% of LLN (Figs. 2–4). The area of uncertain nerve pathophysiology is reflected in diagrams for pathophysiological interpretation of NCS developed by the ESTEEM group (Fig. 1) (Tankisi et al., 2005).

*3.1.1. Demyelination at the nerve level*

*(A)* Motor conduction velocity (CV)/distal motor latency (DML)/F-latency

There are several published criteria to define demyelination at the nerve level varying in the suggested limit of motor conduction slowing and whether the degree of CMAP amplitude reduction is taken into account (AAN Ad hoc subcommittee, 1991; Albers, 1993; Barohn et al., 1989; Bromberg, 1991; Buchthal and Behse, 1977; Gilliatt, 1966; Meulstee and van der Meché, 1995).

As most of these criteria are given as percentage of LLN or ULN, we have attempted to calculate or estimate percentage of deviation from mean, or standard deviation from mean, used in other suggested guideline criteria into percentage of LLN or ULN in Figs. 2–4. In this way a more direct comparison of the different published guidelines is possible. It seems that stricter criteria for demyelination are often required in CIDP than in acute inflammatory demyelinating polyradiculopathy (AIDP). The published criteria require a CV of less than 65% to 80% of LLN in CIDP versus 65% to 90% in AIDP (Fig. 2), and a DML of more than 125% to 150% of ULN in CIDP versus 110% to 150% in AIDP (Fig. 3). In contrast F-latency criteria are within the same range for CIDP and AIDP, i.e. 120–150% of ULN (Fig. 4). The ESTEEM group has suggested the following limits for definite demyelination: >5.5 SD decrease in sensory or motor CV, >8 SD increase in DML or F-wave latency and for probable demyelination: >4.5 SD decrease in CV, >6 SD increase in DML or >8 SD increase in F-wave latency (Fig. 2) (Tankisi et al., 2005). In inherited polyneuropathies a motor CV below 30–38 m/s or a reduction from mean of controls >40% has been suggested as limit for demyelination (Table 3) (Bouche et al., 1983; Buchthal and Behse, 1977; Combarros et al., 1983; Gilliatt, 1966; Harding and Thomas, 1980).

A few studies have examined the relation between NCS and nerve biopsies in CIDP (Barohn et al., 1989; Boukhris et al., 2004; Dyck et al., 1975; McCombe et al., 1987). Motor nerve conduction slowing did not predict the finding on sural nerve biopsy (Barohn et al., 1989). This is in contrast to the more clear-cut relation between sensory slowing and sural biopsy findings in hereditary polyneuropathies (Buchthal and Behse, 1977).

*(B)* Distal CMAP duration and temporal dispersion

An increase in distal CMAP duration has been suggested as a criterion for inflammatory demyelination (Cleland et al., 2003, 2006; Thaisetthawatkul et al., 2002) with the limit of $\geqslant$9 ms suggested by a consensus group (EFNS-PNS Task Force, 2005). In the recent revision of the guidelines the limits were graded for different nerves using the following limits for the interval between onset of first negative peak and return to baseline of the last negative peak: median $\geqslant$6 ms, ulnar $\geqslant$6.7 ms, peroneal $\geqslant$7.6 ms, tibial $\geqslant$8.8 ms (EFNS-PNS Task Force, 2010). Temporal dispersion can be defined as the duration of the CMAP evoked at proximal stimulation compared to the distally evoked CMAP. Two different criteria for demyelination have been suggested: (1) $\geqslant$15% increase in tem-

**Table 3**
Suggested limits for demyelination in hereditary polyneuropathy.

| | CV | % reduction from mean of controls | SD reduction from mean of controls | Nerves | Sural biopsy |
|---|---|---|---|---|---|
| | *Motor conduction velocity* | | | | |
| Gilliatt (1966) | – | >40% | – | All | No |
| Buchthal and Behse (1977) | – | >40% | – | Peroneal, Median | Yes |
| Harding and Thomas (1980) | <38 m/s | – | – | Median | No |
| Bouche et al., 1983 | <30 m/s | – | – | Median | Yes |
| Combarros et al. (1983) | <35 m/s | – | – | Peroneal, Median | Yes |
| Tankisi et al. (2005) | – | >34–42% | >4.5[a] – 5.5[b] SD | All | No |
| | *Sensory conduction velocity* | | | | |
| Buchthal and Behse (1977) | <32 m/s | >40% | – | Sural, Peroneal, Median | Yes |
| Combarros et al. (1983) | <35 m/s | – | – | Peroneal, Median | Yes |
| Tankisi et al. (2005) | – | >35–48% | >4.5[a] – 5.5[b] SD | All | No |

[a] Definite demyelination.
[b] Probable demyelination.

poral dispersion (AAN Ad hoc subcommittee, 1991; Asbury and Cornblath, 1990; Hughes et al., 2001; Nicolas et al., 2002) and (2) ⩾30% increase in temporal dispersion (Albers et al., 1985; Albers and Kelly, 1989; EFNS-PNS Task Force, 2005; Ho et al., 1995; The Italian Guillain-Barre Study Group, 1996; Van den Bergh and Pieret, 2004).

A recent study of the sensitivity in CIDP and specificity versus ALS and diabetic neuropathy suggested distal CMAP duration as a useful index for detection of distal demyelination (Isose et al., 2009), while another study showed that although increased distal CMAP duration and increased proximal to distal CMAP dispersion were more common in hereditary demyelinating neuropathies, these parameters cannot be used in isolation to distinguish acquired from hereditary demyelination (Stanton et al., 2006).

*(C)* Motor conduction block

Several criteria for conduction block of motor fibres have been published. These criteria require a decrease in amplitude or area for proximal CMAP relative to distal CMAP ranging from >20% to 60%, with the certainty of the block often depending on the degree of temporal dispersion (AAN Ad hoc subcommittee, 1991; Barohn et al., 1989; EFNS-PNS Task Force, 2005; Feasby et al., 1985; Lewis et al., 1982; Olney, 1999; Sumner, 1997; Uncini et al., 1993). The criteria suggested by AAEM (Olney, 1999) are the most detailed and conservative (Fig. 5).

*(D)* Sensory CV

The role of sensory NCS in demyelinating neuropathy is not examined in depth (Bragg and Benatar, 2008; Krarup and Trojaborg, 1996; Rajabally and Narasimhan, 2007), and more studies may be useful. A sensory CV less than 32–35 m/s or a 40% decrease from mean of controls has been suggested as limits for demyelination in hereditary polyneuropathy (Table 3) (Buchthal and Behse, 1977; Combarros et al., 1983), while the ESTEEM group has suggested decreases of 5.5 SD and 4.5 SD as limits for definite and probable demyelination, respectively (Fig. 1) (Tankisi et al., 2005). In the AAN criteria for CIDP, a sensory CV less than 80% of LLN is only used as a supportive criterion for sensory demyelination (AAN Ad hoc subcommittee, 1991).

As the peripheral motor nerves are often more affected than the sensory nerves in CIDP, the motor studies may seem more important than the sensory studies. Another factor is the insensitivity of surface recordings of sensory nerves which is the most commonly used technique. If near nerve technique is used, information about CV can be obtained even if there is a great loss of amplitude due to axonal loss or due to temporal dispersion while these changes may be obscured due to an absent response using surface recording (Johnsen and Fuglsang-Frederiksen, 2000).

### 3.1.2. Axonal loss at the nerve level

A decrease in CMAP amplitude with distal stimulation, e.g. of more than 80% of LLN, and no electrophysiological signs of demyelination present evidence of axonal degeneration in motor axonal pol-

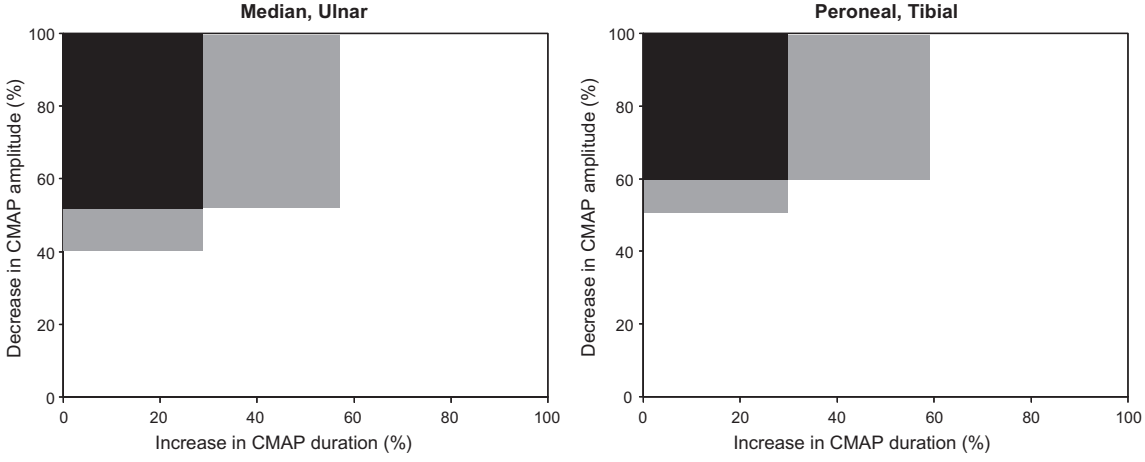


**Fig. 5.** Motor conduction block. Percentage change from proximal to distal stimulation in CMAP amplitude (*x*-axis) and in CMAP duration (*y*-axis) delimit areas corresponding to definite (■) or probable (■) conduction block in the median and ulnar nerves and in the peroneal and tibial nerves. Modified from Olney (1999). Reprinted from Johnsen and Fuglsang-Frederiksen (2000) and Tankisi et al. (2005) with permission from Elsevier.

**Table 4**
Electrophysiological criteria for diagnosis of definite CIDP.

| AAN (1991) | Hughes et al. (2001) | EFNS-PNS (2005, 2010) | Koski et al. (2009)[d] |
|---|---|---|---|
| *Electrodiagnostic criteria* | | | |
| Three of the following four criteria[a] should be fulfilled in motor nerves | One of the following three criteria should be fulfilled in motor nerves | Definite CIDP requires one of the following criteria in motor nerves | Recordable response in at least 75% of motor nerve tested and one of the following criteria |
| • 2 nerves with abnormal CV, DML or F-waves[a]<br>• 1 nerve in forearm or leg with partial CB or abnormal TD 2 nerves with abnormal DML[a]<br>• 2 nerves with abnormal F-waves (absent or significant increased latency) | • 2 nerves with CB or TD, 1 nerve with abnormal CV, DML or F-waves[a]<br>• 3 nerves with abnormal CV, DML or F-waves[a]<br>• 2 nerves with abnormal CV, DML or F-waves[a] and sural nerve biopsy with significant sign of demyelination | • 2 nerves with abnormal DML[b]<br>• 2 nerves with abnormal CV[b] 2 nerves with abnormal F-wave latency[b]<br>• 2 nerves with absent F-waves[b], 1 other nerve with $\geqslant 1$ other demyeli-nating parameter<br>• 2 nerves with partial CB[b] or 1 nerve with partial CB[b], 1 other nerve with $\geqslant 1$ other demyeli-nating parameter<br>• 2 nerves with abnormal TD[b]<br>• 1 nerve with abnormal distal CMAP duration[b], 1 other nerve with $\geqslant 1$ other demyeli-nating parameter | • Abnormal DML[a] in > 50% of motor nerves tested Abnormal CV[a] in > 50% of motor nerves tested<br>• Abnormal F-latency[a] in > 50% of motor nerves tested<br>Or<br>Clinical criteria part B |
| *Clinical, pathological and laboratory criteria*[c] | | | |
| • Motor and/or sensory dysfunction of more than one limb<br>• Development over >2 months<br>• Hypo- or areflexia. Usually affecting all four limbs<br>• Nerve biopsy showing unequivocal evidence of de- and remyelination<br>• Cell count <10/mm$^3$, negative VDRL | • Progressive or relapsing motor and sensory dysfunction of more than one limb resulting from neuropathy<br>• Development over >2 months<br>• Reduced or absent tendon reflexes<br>• Significant disability in upper or lower limb function (at least arm disability grade 2 or leg disability grade 1) | • Chronically progressive, stepwise, or recurrent symmetric proximal and distal weakness and sensory dysfunction of all extremities; cranial nerves may be affected<br>• Development over >2 months<br>• Absent or reduced tendon reflexes in all extremities | A • No serum paraprotein<br>• No genetic abnormality<br>• Duration >8 weeks |
| | | | B • Symmetrical onset or symmetrical examination<br>• Weakness in all four limbs<br>• At least one limb with proximal weakness |

[a] Significant change see AAN ad Hoc Subcommittee (1991), pages 9–10, and Figs. 3–5.
[b] Significant change see EFNS-PNS (2010), pages 9–10, and Figs. 3–5.
[c] Mandatory for typical CIDP.
[d] Clinical criteria part A and electrodiagnostic criteria or clinical criteria part B required.

**Table 5**
Electrophysiological criteria for diagnosis of polyneuropathy suggested by the ESTEEM group (Tankisi et al., 2005).

| Demyelinating polyneuropathy | Axonal polyneuropathy | Mixed polyneuropathy |
|---|---|---|
| *Electrodiagnostic criteria*[a] | | |
| • 2 nerves with definite demyelination or 1 nerve with definite demyelination and 2 nerves with probable demyelination or 4 nerves with probable demyelination<br>• Affection in >2 extremities | • 2 sensory or motor nerves with axonal loss[b]<br>• Affection in >2 extremities<br>• Criteria for demyelinating polyneuropathy not fulfilled | • 2 nerves with definite demyelination or 1 nerve with definite demyelination and 2 nerves with probable demyelination or 4 nerves with probable demyelination<br>• 2 sensory or motor nerves with axonal loss[b]<br>• Demyelination and axonal loss must be found in different nerves<br>• Affection in >2 extremities |

[a] For criteria defining demyelination and axonal loss at the nerve level see Tankisi et al. (2005).
[b] Results from motor nerve studies with low CMAP amplitude can only be used if myopathy or neuromuscular transmission disorders have been excluded.

yneuropathy (Hadden et al., 1998; Ho et al., 1997; Van der Meché et al., 2001). The ESTEEM group has suggested a >2.5 SD decrease in SNAP or CMAP amplitude with normal or near normal, i.e. <2.5 SD decreased, CV as a criterion for axonal loss (Fig. 1) (Tankisi et al., 2005). It should, however, be kept in mind that decreased CMAP amplitude may also be seen in myopathies and neuromuscular transmission disorders and is therefore not a specific characteristic of axonal damage. Additionally, reinnervation by collateral sprouting may cause the CMAP amplitude to be normal or much less reduced than what would be expected from the loss of motor axons. In such cases, EMG or motor unit number estimation (MUNE) should supplement the study to evaluate the possible loss of motor axons.

#### 3.1.3. Patient level

Most protocols for electrophysiological examination of polyneuropathy require examination of motor and sensory nerves in at least two extremities (American Association of Electrodiagnostic Medicine, 1992). Some studies suggest at least two (Saperstein et al., 2001) or three (AAN Ad hoc subcommittee, 1991; Asbury and Cornblath, 1990; Hughes et al., 2001) different abnormal parameters in at least two nerves, while only one abnormal parameter in each of at least two different nerves is required in other criteria (Meulstee and van der Meche, 1995; Tankisi et al., 2005; Van den Bergh and Pieret, 2004). To our knowledge there are no evidence-based studies on this topic.

### 3.2. Inflammatory demyelinating neuropathies

There exists a huge amount of literature on diagnostic criteria for CIDP and AIDP, both from different laboratories and from more official consensus groups such as AAN (AAN Ad hoc subcommittee, 1991), INCAT (Hughes et al., 2001), EFNS (EFNS-PNS Task Force, 2005, 2010), the French CIDP Study Group (French CIDP Study Group, 2008) and Koski et al. (Koski et al., 2009).

#### 3.2.1. Chronic inflammatory demyelinating polyradiculoneuropathy (CIDP)

Although a typical profile for CIDP was described already by Dyck et al. (1975), precise criteria for diagnosing CIDP were first described later by Barohn et al. (1989). Several diagnostic criteria have been proposed later, but only a handful of these are developed by expert consensus groups (Table 4) (AAN Ad hoc subcommittee, 1991; EFNS-PNS Task Force, 2010; Hughes et al., 2001; Koski et al., 2009). The first consensus criteria were developed for research purposes by an ad hoc subcommittee of the American Academy of Neurology (AAN) and are rather detailed and restrictive with the risk of missing some patients (AAN Ad hoc subcommittee, 1991). The criteria suggested later by the Joint Task Force of the EFNS and PNS (EFNS-PNS Task Force, 2005) and recently revised (EFNS-PNS Task Force, 2010), were derived by a consensus group including systematic reviews of literature, and were slightly less restrictive than the AAN criteria. The criteria for diagnosing patients suggested by INCAT (Hughes et al., 2001) and ESTEEM (Table 5) (Tankisi et al., 2005) seem simpler, but also easier to use in the daily routine.

Only the diagnostic criteria by Koski et al. were developed by an expert consensus group in combination with a data-driven approach (Koski et al., 2009). With these rather simple criteria at patient level the sensitivity (83%) and the specificity (97%) were higher or at the same level as when earlier consensus criteria were applied on the same patient groups, i.e. a group of other chronic acquired demyelinating polyneuropathy patients and a group of other polyneuropathy patients, apart from the CIDP patients. The authors suggest that either a set of clinical criteria or a set of electrophysiological criteria can be used for diagnosing CIDP. If only their electrophysiological criteria are used, the sensitivity will probably be much less.

*Comments:* In general the diagnostic criteria in CIDP defined by the earlier consensus groups in the 1990s were rather restrictive and with time were made less restrictive by later consensus groups. The high specificity in the early restrictive criteria may be appropriate in research of treatment effect in patient groups where a definite diagnosis is essential. However, in electrodiagnostic studies of individual patients a higher sensitivity may be required in order not to miss the diagnosis of a potential treatable disorder. To group the patients into definite, probable, and possible CIDP depending on the strength of the electrodiagnostic criteria seems a practical solution in order to handle the uncertainty met in the daily examinations as well as research projects (Laughlin et al., 2009; EFNS-PNS Task Force, 2010).

#### 3.2.2. Acute inflammatory demyelinating polyradiculoneuropathy (AIDP)

There is a great number of suggested electrophysiological criteria for AIDP (Asbury and Cornblath, 1990; Albers et al., 1985; Hadden et al., 1998; Ho et al., 1995; Kalita et al., 2008; Meulstee and van der Meche, 1995; The Italian Guillain-Barre Study Group, 1996; Van den Bergh and Pieret, 2004). In contrast, no criteria have been developed by an official consensus group of experts selected by scientific society. Often the criteria for AIDP are less stringent than the criteria for CIDP (Figs. 3 and 4) and the sensitivity is high. For three sets of criteria (Albers et al., 1985; Ho et al., 1995; Meulstee and van der Meche, 1995) compared in groups of patients the sensitivity varied from 82% to 89% (Kalita et al., 2008; Van den Bergh and Pieret, 2004). For these sets the specificity against ALS patients was high, however, the specificity against distal polyneuropathy was low (Van den Bergh and Pieret, 2004).

*Comments:* The high sensitivity of the criteria facilitates the use of IVIg or plasmapheresis to treat patients suspected of AIDP.

#### 3.2.3. Multifocal motor neuropathy

Criteria for the diagnosis of multifocal neuropathy has been suggested by a consensus group (Table 6) (Olney et al., 2003).

**Table 6**
Criteria for the diagnosis of multifocal motor neuropathy (MMN) (Olney et al., 2003).

| |
|---|
| *Definite MMN* |
| Weakness without objective sensory loss in the distribution of ⩾2 nerves. No diffuse, symmetric weakness during the early stages of symptomatic weakness |
| Definite CB[a] in ⩾2 motor nerves outside of common entrapment sites[b] |
| Normal sensory CV across the segments with demonstrated motor CB[a] |
| Normal sensory NCS on all tested nerves with ⩾3 nerves tested |
| Absence of following UMN signs: spastic tone, clonus, extensor plantar response, and pseudobulbar palsy |
| *Probable MMN* |
| Weakness without objective sensory loss in the distribution of ⩾2 nerves. No diffuse, symmetric weakness during the initial weeks of symptomatic weakness Presence of either: |
| a. Probable CB[a] in ⩾2 motor nerve segments that are not common entrapment sites* |
| b. Definite CB[a] in 1 motor nerve segment and probable CB[a] in a different motor nerve segment, neither of which are common entrapment sites[b] |
| Normal sensory CV across the segments with demonstrated motor CB[a], when technically possible (i.e. not required for segments proximal to axilla or popliteal fossa) |
| Normal results for sensory NCS on all tested nerves with ⩾3 nerves tested |
| Absence of following UMN signs: spastic tone, clonus, extensor plantar response, and pseudobulbar palsy |

[a] As defined by Olney (1999).
[b] Median nerve at wrist; ulnar nerve at elbow or wrist; peroneal nerve at fibular head.

### 3.3. Axonal polyneuropathy

To our knowledge only a few studies concern criteria for acquired axonal polyneuropathy. At patient level some authors state that if a polyneuropathy is not demyelinating, it is axonal (Hughes et al., 2001; Hughes, 2002; Logigian et al., 1994; Rosenberg et al., 2001). This reasoning is probably too simple, on the one side because of the grey zone described above and on the other side because a mixed polyneuropathy, i.e. with demyelination in some nerves and axonal loss in other nerves, may exist. One consensus group have suggested criteria for primarily axonal polyneuropathy (Table 5) (Tankisi et al., 2005).

### 3.4. Mixed polyneuropathy

A mixed polyneuropathy is not very well described in the literature and there are only few guidelines for the classification of mixed polyneuropathy requiring demyelination of some nerves and axonal loss in other nerves (Donofrio and Albers, 1990; Tankisi et al., 2005). The guidelines for classification of a mixed polyneuropathy from the ESTEEM group are listed in Table 5.

*Comments:* Mixed polyneuropathy may not be the most appropriate term, as even a demyelinating polyneuropathy almost always has mixed features with primary demyelination and associated axonal loss at the nerve level, which may lead to confusion (Dyck et al., 1971; Behse and Buchthal, 1977; Johnsen and Fuglsang-Frederiksen, 2000). Occasionally, the term mixed polyneuropathy is incorrectly used to describe a polyneuropathy that cannot be classified due to uncertain findings corresponding to the grey zone without clear evidence of the pathophysiology (Tankisi et al., 2005). The clinical relevance of a mixed polyneuropathy is unknown.

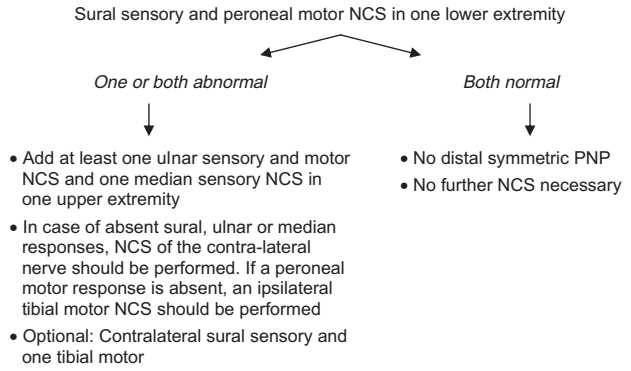


**Fig. 6.** Examination strategy for distal symmetric polyneuropathy (England et al. 2005).

### 3.5. Distal symmetric polyneuropathy

In a recent paper concerning AANEM practice parameters for distal symmetric polyneuropathy, electrodiagnostic examination is used to differentiate between axonal and demyelinating pathology solely (England et al., 2009), while another consensus paper from AAEM suggests electrodiagnostic findings to be included "as part of the case definition" and suggests a protocol for NCS and minimal criteria for the electrodiagnosis: an abnormality of any attribute of nerve conduction in two separate nerves, one of which must be the sural nerve (Fig. 6) (England et al., 2005).

### 3.6. Hereditary polyneuropathy

At present there are no consensus electrodiagnostic criteria for hereditary polyneuropathy. Generally speaking, uniform demyelination favours an inherited neuropathy, whereas patchy findings with differences between nerves, and segments within a nerve are more in favour of an acquired syndrome (Willison and Winer, 2003). Conduction block and increased temporal dispersion are features of focal demyelination and may therefore help to discriminate between acquired and hereditary demyelinating polyneuropathy. As exceptions should be mentioned hereditary neuropathy

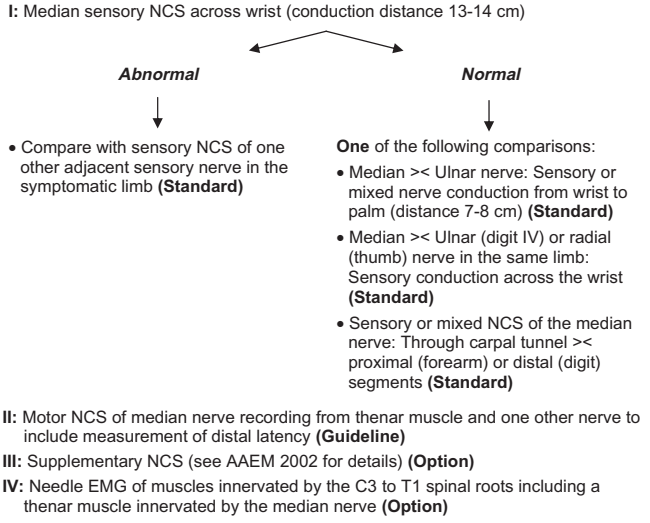


**Fig. 7.** Examination strategy for suspected carpal tunnel syndrome (AAEM, 2002).

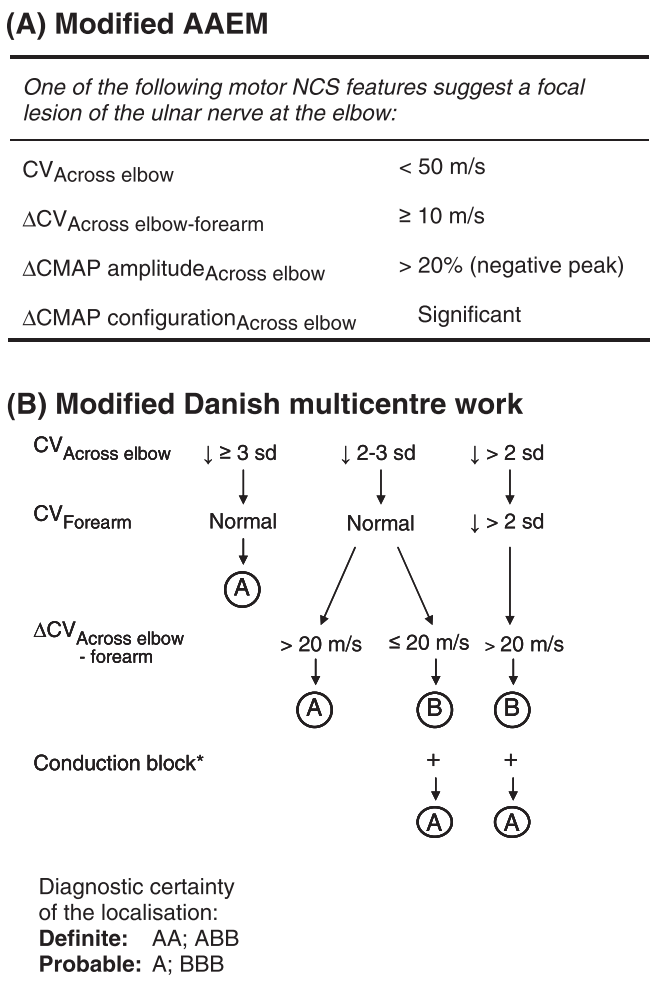


**Fig. 8.** Guidelines for localisation of ulnar lesion at elbow. Part A is modified from the guidelines from AAEM and Campbell (1999). Part B is modified from the work by a Danish consensus group (unpublished). In the latter guidelines, a certainty of A or B is assigned to each NCS of the ulnar nerve across the elbow, with A being more certain than B. A total score for the certainty of an ulnar lesion localised at the elbow is obtained by combining the assigned certainties. AA or ABB suggest a definite focal lesion of ulnar nerve at elbow, A or BBB suggest a probable focal lesion of ulnar nerve at elbow. If CMAP amplitude is <0.5 mV, A changes to B, and B is cancelled. *See Olney (1999).

with liability to pressure palsies (HNPP) and X-linked Charcot–Marie–Tooth disease (CMTX), which may be asymmetrical and show uneven slowing of conduction (Andersson et al., 2000; Birouk et al., 1998; Gutierrez et al., 2000).

### 3.7. Nerve entrapment

#### 3.7.1. Carpal tunnel syndrome

In 1993 AAEM first published evidence-based practice parameters for electrodiagnostic studies in carpal tunnel syndrome (AAEM, 1993), which later were modified (Fig. 7) (AAEM, 2002). These practice parameters suggest diagnostic examination strategies,

#### 3.7.2. Localisation of ulnar nerve lesion at elbow

A consensus paper by AAEM suggests several localising parameters with only rather small changes required for accepting a localised lesion (AAEM and Campbell, 1999) while a Danish consensus group are using much more rigorous criteria (Fig. 8) (unpublished). Here each study of the ulnar nerve is assigned a certainty according to the suggested limits of ulnar CV in the forearm and across the elbow. In this way, addition of studies of the ulnar nerve, either motor studies with recording in different muscles or sensory studies examined using the near-nerve needle technique across the elbow, can increase the diagnostic certainty of the localisation.

**Table 7**
Electrodiagnostic criteria for tarsal tunnel syndrome. Tests confirming the presence of tibial mononeuropathy at the level of the tarsal tunnel when the possibility of a polyneuropathy has been excluded (Patel et al., 2005).

| Test | Criteria |
|---|---|
| Tibial motor NCS | Increased DML |
| Medial and lateral plantar sensory NCS | Slowed CV across tarsal tunnel and/or small SNAP amplitude Absent responses |
| Medial and lateral plantar mixed NCS | Prolonged peak latency Slowed CV across tarsal tunnel |

#### 3.7.3. Tarsal tunnel syndrome

An AANEM consensus group have published recommendations for electrodiagnostic criteria for the diagnosis of tarsal tunnel syndrome (Patel et al., 2005). The authors reviewed 319 articles. Only three of these met six of their inclusion criteria and one met five criteria. The recommendations given in Table 7 meet the evidence-based grading of Level C Class III. The sensitivity and specificity could not be determined, though.

#### 3.7.4. Peroneal neuropathy

The AAEM practice parameter for patients with suspected peroneal neuropathy presents evidence-based sensitivity of the electrodiagnostic examination build on 11 studies meeting the literature inclusion criteria (Marciniak et al., 2005). It was concluded that there was class III evidence (six studies) or class IV evidence (five studies) in support of a role for NCS in diagnosing peroneal neuropathy, and that the use of electrodiagnostic medicine in these patients is recommended (level C). It was further suggested that a consensus-based reference standard for the clinical diagnosis should be developed.

### 3.8. Cervical radiculopathy

A consensus paper from AAEM suggests guidelines for the diagnosis of cervical radiculopathy using EMG and NCS (AAEM, 1999b). EMG and NCS are suggested to be used to delineate the muscles innervated by a specific root and to exclude differential diagnoses (Table 8). There is no information about which muscles are innervated by which root.

There are no consensus guidelines on brachial plexus lesions, which are an important differential diagnosis to cervical radiculopathy. Neither do consensus guidelines on lumbosacral radiculopathy exist.

**Table 8**
Electrodiagnostic criteria for cervical radiculopathy (AAEM, 1999b).

| Symptomatic limb |
|---|
| *Nerve conduction studies* |
| • ⩾1 motor and ⩾1 sensory NCS to exclude PNP and entrapment |
| • If symptoms and signs suggest CTS, ulnar neuropathy or PNP or ⩾abnormal NCS more studies should be performed |
| *Electromyography* |
| • ⩾1 muscle at the C5, C6, C7, C8 and T1 levels |
| • Paraspinal muscles at ⩾1 level |
| *If specific root suspected clinically or abnormality seen at initial EMG examination* |
| • ⩾1 additional muscle innervated by that root and a different nerve |
| • Demonstration of normal muscle above and below the root |

**Table 9**
Clinical and electrodiagnostic criteria for the diagnosis of ALS. Part A outlines the revised El Elscorial criteria (Brooks et al., 2000) and part B the EMG criteria for the diagnosis of ALS (Brooks et al., 2000; de Carvalho et al., 2008). Both active and chronic denervation findings are required, but the relative proportion may vary from muscle to muscle.

| (A) Diagnostic criteria | | | | |
|---|---|---|---|---|
| Presence of<br>LMN degeneration<br>UMN degeneration<br>Progressive spread of symptoms and signs | | Absence of<br>Electrophysiological, pathophysiological, and neuroimaging results explaining clinical signs | | |
| Diagnostic categories | | Number of regions affected | | |
| | | LMN[a] | UMN | |
| Definite | | 3 | 3 | |
| Probable | | 2 | 2 (partly above LMN signs) | |
| Possible | | 1 | 1 (same as LMN) | |
| | | 1 | 1 (below LMN) | |
| | | 0 | ⩾2 | |
| Suspected[b] | | ⩾2 | 0 | |
| (B) EMG criteria | | | | |
| Sign of chronic denervation | | Sign of active denervation | Requirements per region | |
| Qualitative EMG | Quantitative EMG | Fibrillation potentials | Region | Required muscles |
| MUP analysis: large individual MUPs, unstable MUPs | Neurogenic changes on: quantitative MUP analysis, Quantitative IP analysis, MUNE, Macro EMG, or Single fibre EMG | Positive sharp waves | Brainstem | ⩾1 |
| IP analysis: discrete pattern with increased amplitude or reduced pattern with firing rates higher than 10 Hz and no UMN component | | Fasciculation potentials[c] | Cervical | ⩾2[e] |
| | | | Lumbosacral | ⩾2[e] |
| | | | Thoracic spinal cord[d] | ⩾1 |

[a] LMN signs defined by clinical or electrophysiological evidence according to the Awaji-Shima consensus recommendations (de Carvalho et al., 2008).
[b] The authors of this review suggest this category to be included in studies of initial progression of ALS.
[c] In the presence of chronic denervation (de Carvalho et al., 2008).
[d] Paraspinal muscle below T6 level or abdominal muscle.
[e] Different peripheral nerves innervated by different roots.

### 3.9. Amyotrophic lateral sclerosis (ALS)

Electrodiagnostic studies are recommended to support the clinical diagnosis of ALS for two main purposes: first, to confirm denervation in clinically involved regions and corroborate the diagnosis of ALS by detecting denervation changes in clinically unaffected muscles, and second, to rule out other disorders of the peripheral nervous system mimicking ALS (Brooks, 1994).

The first electrodiagnostic criteria for the diagnosis of ALS was made by Lambert who listed a combination of four electrodiagnostic findings that he considered highly supportive for the clinical diagnosis of ALS (Lambert, 1969). The World Federation of Neurology Subcommittee on Motor Neuron Disease made new criteria for the diagnosis of ALS in 1990 in El Escorial, Spain (Brooks, 1994) and formulated new electrodiagnostic criteria, presumably because the Lambert criteria were considered too stringent, with only patients with rather advanced disease likely to satisfy them (Behnia and Kelly, 1991). However, the electrodiagnostic portion of the El Escorial criteria (EEC) was considered to be confusing and to contain several flaws, which limited their use by electrodiagnostic physicians (Wilbourn, 1998). In the revision of the El Escorial criteria in Airlie House in 1998 (Brooks et al., 2000), the electrodiagnostic criteria were again made less specific. The revised El Escorial diagnostic criteria are still the most commonly used criteria in clinical studies and therapeutic trials in patients with ALS, and although helpful, are considered not to be sufficiently sensitive and having problems in detecting lower motor neuron signs and favouring clinical signs more than electrodiagnostic findings (Beghi et al., 2002; Chaudhuri et al., 1995; Ross et al., 1998; Traynor et al., 2000). To overcome this, a consensus group suggested some helpful modifications to the revised El Escorial Criteria at an IFCN sponsored consensus conference on Awaji Island in 2006 (de Carvalho et al., 2008). The main suggestions of the Awaji Group were first to incorporate electrophysiological signs of LMN dysfunction equally to clinical signs in the definite, probable and possible diagnosis of ALS and second to interpret the presence of fasciculation potentials as an expression of acute denervation equivalent to that of fibrillation potentials and positive sharp waves.

The revised El Escorial criteria for the diagnosis of ALS including the Awaji group's recommendations are outlined in Table 9. In summary, the criteria are based on four body regions: the brainstem region, the cervical and lumbosacral spinal cord regions, and the thoracic spinal cord region, and the diagnosis is categorised into three levels of certainty depending on the number of regions with UMN or LMN signs. For EMG-findings to support the diagnosis of ALS, signs of chronic and active denervation should be found in at least two muscles in the cervical and lumbosacral spinal cord regions and in one muscle in the brainstem and thoracic spinal cord regions (Table 9).

*Comments:* The revised El Escorial criteria with the addition of the Awaji Group's recommendation on EMG have increased the utility of using diagnostic criteria in ALS (Fuglsang-Frederiksen, 2008). However, the authors of this review find it rather difficult to read and apply these criteria in the daily clinic. It should be possible to present these criteria in a simpler way and we therefore call for a consensus group of experts to develop such a set of criteria.

The diagnostic guidelines for ALS require normal sensory NCS. However, minor sensory abnormalities are often encountered in ALS and should be allowed (Hammad et al., 2007; Pugdahl et al., 2007, 2008). In case of a suspicion of polyneuropathy in addition to ALS we suggest that the diagnostic criteria should stress that follow-up studies are needed.

Another point in diagnosing ALS is the lack of objective sensitive and specific methods to diagnose upper motor neuron lesion. However, this requires more evidence-based studies of existing or new methods.

**Table 10**
Guidelines for the diagnosis of neuromuscular transmission failure. Studies must be performed in a symptomatic muscle, skin temperature ⩾35 °C, anti-acetylcholinesterase withdrawn ⩾12 h before examination. AAEM, 2001.

| Test | Criteria |
|---|---|
| *Repetitive nerve stimulation* | |
| 2–5 Hz stimuli baseline | ⩾10% decrement of AP amplitude from stimulus 1 to 4/5 |
| 2–5 Hz stimuli post exercise/post titanic every ½-1 min up to 5 min | ⩾100% post exercise/tetanic increase in AP amplitude (abnormality in LEMS) |
| *Single fibre EMG* | |
| AP pairs (amplitude > 200 μV, rise time < 300 μs) | >10% pairs increased individual jitter or blocking and/or increased mean jitter (MCD) |

LEMS, Lambert-Eaton myasthenic syndrome; AP, action potential; MCD, mean consecutive differences.

### 3.10. Muscular disorders

There exists a huge amount of literature concerning the sensitivity and specificity of different electrophysiological methods for detecting myopathic changes in the muscle (Buchthal, 1991; Daube and Rubin, 2004; Fuglsang-Frederiksen, 2006). However, no proper evidence-based guideline for examination strategy or diagnostic strategy exists. Guidelines would probably increase the quality of the electrophysiological examination in myopathy as there is a great variation among physicians in techniques used and qualitative versus quantitative methods (Fuglsang-Frederiksen et al., 1995; Johnsen et al., 1994).

Neither are there any consensus guidelines for electrophysiological diagnosing of different types of muscular channelopathies.

### 3.11. Neuromuscular transmission failure

Guidelines for the examination of patients with repetitive nerve stimulation (RNS) and single fibre EMG (SFEMG) and diagnostic criteria for myasthenia gravis (MG) and Lambert-Eaton myasthenic syndrome (LEMS) (Table 10) were suggested by a consensus group under the auspices of AAEM (AAEM Quality Assurance Committee, 2001). The guidelines were built on a literature search and the literature was graded for classification of evidence A–C obtained from literature classification criteria 1–6.

These guidelines seem somewhat simple, they do not take into account the clinical picture, the distribution of affected muscles or the severity of the affection, i.e. borderline versus significant changes, neither do they consider the utility of high frequency stimulation for diagnosing LEMS.

## 4. Conclusion

In the field of standards and guidelines for electrodiagnosis of neuromuscular disorders, the authors of this review ask for future diagnostic studies using evidence-based medicine principles as outlined by AANEM and the STARD initiative, as well as outcome or cost-benefit studies.

In order to optimise the electrodiagnostic examination of patients with neuromuscular disorders, continuous quality improvement is needed, not only at national or society level, but also at the individual laboratory level. This includes medical audit and implementation of examination strategies and diagnostic guidelines in the daily routine.

With respect to guidelines there is an abundance concerning inflammatory demyelinating neuropathies; several of these are developed by international expert consensus groups. The development of these guidelines is often driven by the aim of selecting patients for treatment trials and they are therefore rather restrictive with respect to ensuring the diagnosis, perhaps more than needed to diagnose the individual patient in the laboratories. Also the diagnostic guidelines for ALS patients are aiming for selection of patients for research and test of potential treatment drugs more than the routine use in the EMG laboratory. The problem with the ALS guidelines, both the earlier El Escorial criteria, the revised El Escorial criteria and the supplementary Awaji criteria is that they are complicated to read and therefore may also be difficult to use in a uniform way in a multicentre study as well as in the individual laboratory.

With respect to guidelines for other kinds of neuromuscular disorders they are sparse or non-existent.

In other words, guidelines for polyneuropathy and ALS could be more precise and easier to communicate, while guidelines for most other kinds of neuromuscular disorders need to be developed or optimised.

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