Advances in management of Guillain–Barré syndrome

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Purpose of review
The clinical presentation of Guillain–Barré syndrome (GBS) is highly variable, which can make the diagnosis challenging. Intravenous immunoglobulin (IVIg) and plasma exchange are the cornerstones of treatment since decades. But despite these treatments, 25% initially progress in muscle weakness, 25% require artificial ventilation, 20% is still not able to walk independently after 6 months, and 2–5% die, emphasizing the need for better treatment. We summarize new developments regarding the diagnosis, prognosis, and management of GBS.

Recent findings
GBS is a clinical diagnosis that can be supported by cerebrospinal fluid examination and nerve conduction studies. Nerve ultrasound and MRI are potentially useful techniques to diagnose inflammatory neuropathies. Several novel infections have recently been associated to GBS. Evidence from experimental studies and recent phase 2 clinical trials suggests that complement inhibition combined with IVIg might improve outcome in GBS, but further studies are warranted. Prognostic models could guide the selection of patients with a relatively poor prognosis that might benefit most from additional IVIg or otherwise intensified treatment.

Summary
New diagnostic tools may help to have early and accurate diagnosis in difficult GBS cases. Increased knowledge on the pathophysiology of GBS forms the basis for development of new, targeted, and personalized treatments that hopefully improve outcome.

Keywords
complement inhibition, Guillain–Barré syndrome, MRI, nerve ultrasound, preceding infections

INTRODUCTION
Guillain–Barré syndrome (GBS) is an acute onset immune-mediated polyradiculoneuropathy characterized by a rapidly progressive, bilateral weakness of the limbs and hypo- or areflexia [1,2]. Weakness is often accompanied by sensory symptoms, and both cranial and autonomic nerve fibers can also be involved [3]. Pain may precede the onset of weakness [3,4]. Several clinical variants can be distinguished, such as the Miller Fisher syndrome (MFS), the pharyngeal-cervical-brachial variant, and paraparetic GBS [3]. Because the presentation is highly variable, the diagnosis can be challenging in clinical practice. The diagnosis can be supported by cerebrospinal fluid (CSF) examination and/or nerve conduction studies (NCS). Based on NCS, two main subtypes of GBS can be distinguished: acute inflammatory demyelinating polyradiculoneuropathy (AIDP) and acute motor axonal neuropathy (AMAN) [3]. However, CSF and NCS findings are normal in a subset of patients, especially early in the course of disease, emphasizing the need for new diagnostic techniques [5**]. Nerve ultrasound and MRI have been suggested as potentially useful diagnostic techniques for GBS [6,7,8,9]. Infections precede GBS in the majority of cases, but other events, such as vaccinations, have also been reported preceding GBS [3,10**]. Identifying the trigger for GBS is important to understand the underlying pathogenic mechanisms, but also to anticipate for a possible rise in incidence following an epidemic or pandemic, as was seen with the recent Zika virus (ZIKV) infection [11*,12*].

Current standard treatment for GBS is intravenous immunoglobulin (IVIg) or plasma exchange, but despite these treatments morbidity and
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KEY POINTS

- Identifying preceding infections and establishing causality with GBS increases knowledge on the epidemiology and pathophysiology of GBS, and additionally allows for anticipation to a rise in incidence of GBS following unusual epidemics.
- Nerve ultrasound is a potentially useful diagnostic tool for GBS in addition to NCS by detecting nerve enlargement in an early phase of disease.
- Contrast-enhanced MRI in GBS can show enhancement and thickening in the cauda equina and nerve roots, and could be helpful to diagnose GBS, especially in atypical cases.
- Complement inhibition constitutes the first potential “targeted therapy” for GBS, and might improve outcome as add-on treatment to IVlg.
- Prognostic models can help to identify patients with a poor outcome in an early stage of disease, which might provide a basis for a more personalized intensified or additional treatment.

mortality is still substantial [3]. Previous experimental findings indicated an important role for antibody-mediated complement activation in the pathogenesis of GBS, providing a basis for therapeutic studies with complement inhibitors as the first “targeted therapy” for GBS [13*,14,15*,16**]. Prognostic models are now available that can be helpful to select patients that may potentially benefit from new treatment modalities [17,18,19*].

In this review we will give an overview of the advances in the management of GBS. The main focus will be on new developments with respect to preceding infections, diagnostic techniques, treatment, and prognosis. Results of recent phase 2 trials with the complement inhibitor eculizumab, and future perspectives regarding an intensified IVlg treatment schedule or other novel therapeutic agents will be discussed.

PRECEDING INFECTIONS AND PATHOPHYSIOLOGY

Extensive progress has been made in understanding how preceding infections result in peripheral nerve damage in GBS, especially in the AMAN subtype. Infections with Campylobacter jejuni, the predominant preceding infection of GBS, may result in the production of cross-reactive antibodies that bind to human peripheral nerve gangliosides, a process that is referred to as “molecular mimicry” [3,10**]. Binding of these antibodies to the peripheral nerves may result in activation of complement, and local deposition of membrane attack complexes and infiltration of macrophages, resulting in disruption of the axonal membrane [3,10**]. The underlying pathogenic mechanism for AIDP seems to be more complex, as in the majority of these patients no antibodies were found. In some patients with AIDP, antibodies were identified to individual gangliosides or ganglioside complexes, but their role in the pathogenesis in these cases is unknown [3].

Various types of infections have previously been associated with GBS [3], but in about half of the cases a preceding infection remains elusive. Recently novel causative agents have been identified. Hepatitis E virus (HEV) infections were found in 5–11% of GBS cases, compared to less than 1% of controls. The definition of an acute HEV infection differed between studies, but was generally based on detecting viral genome or anti-HEV immunoglobulin M (IgM) antibodies in serum, sometimes supported by the presence of anti-HEV immunoglobulin G (IgG) antibodies [20–22,23*,24]. In 75% of GBS patients with anti-HEV IgM seropositivity, liver enzymes were elevated, but this finding indicates that HEV-related GBS may also occur in absence of laboratory signs of hepatitis [21,22,23*]. Mycoplasma pneumoniae has previously been associated to GBS, but only in a small subgroup (<5%) of patients [3,25]. Interestingly, a case-control study recently demonstrated IgM antibodies to M. pneumoniae in 21% of children with GBS, compared to 7% of pediatric controls [26*]. Preceding M. pneumoniae infections were associated with antibodies to galactocerebroside (GalC), and cross-reaction of anti-GalC antibodies was seen with different strains of M. pneumoniae, including an isolate from a GBS patient [26*]. In 2013, a ZIKV outbreak in French Polynesia was followed by a 20-fold increase in GBS cases. A case-control study conducted during the outbreak period found neutralizing antibodies against ZIKV in 100% of GBS cases and 56% of controls [11*]. Since then multiple studies have been performed on the association between ZIKV and GBS, but definitive causality has yet to be established [12*,27*].

At present, the identification of the type of preceding infection in GBS usually has no consequences for therapeutic management. However, some preceding infections are related to specific clinical variants or subtypes of GBS and may influence the prognosis. This could be important in future management of GBS, to predict the clinical course and develop a more individualized treatment approach [3]. In addition, knowing the trigger of GBS may be relevant to prevent cases of GBS in the future [28]. Most infections related to GBS are very common, indicating that host susceptibility factors
probably play an additional role in the pathogenesis. For instance, patients with a C. jejuni-related GBS have an intrinsic higher dendritic cell response to C. jejuni lipo-oligosaccharides than controls [29]. A recent cohort study investigated the role of a functional polymorphism of the neonatal Fc receptor in IVlg pharmacokinetics and disease course of GBS, but did not find any association [30]. More research is needed to gain better insight into the host factors that are involved in GBS.

**DIAGNOSIS**

**Clinical criteria**

The first diagnostic criteria for GBS date from 1978, and were revised in 1990 by Asbury and Cornblath [1]. In 2011, the Brighton Collaboration provided new case definitions for GBS and MFS for vaccine safety monitoring [2]. For the Brighton classification, GBS diagnosis is subdivided into 4 levels of certainty (level 1: highest level of diagnostic certainty; level 4: lowest level of diagnostic certainty) based on clinical symptoms, CSF, and NCS findings. Recently, the Brighton criteria were validated in three independent cohorts of patients with GBS. These studies showed that in patients with a complete dataset level 1 or 2 was reached in 94% of 335 Dutch adult patients, 99% of 220 adult patients from Bangladesh, and in 96% of 46 Dutch children [5,31,32]. The performance of the Brighton criteria is highly dependent on the completeness of data, and is possibly influenced by the timing of hospital admission. In previous validation studies, it was not possible to determine the specificity of the Brighton criteria, because all included patients fulfilled the National Institute of Neurological Disorders and Stroke criteria for GBS and patients with alternative diagnosis were excluded. Owing to the incorporation of both CSF and NCS findings, the Brighton criteria are most likely less suitable for diagnosing GBS with a high level of certainty in the acute phase of disease, because these laboratory findings may then still be normal.

The presentation of GBS in children may differ from adults, and especially young children can be more difficult to examine, which may cause diagnostic delay. As pain is a frequent complaint in children with GBS, it should be taken into account when considering the differential diagnosis [32,33,34].

**Cerebrospinal fluid**

A classical finding of CSF examination in GBS is the albuminocytological dissociation. A large cohort study showed that the CSF protein level is highly dependent on the timing of lumbar puncture. When lumbar puncture was performed within 1 day from onset of weakness, 49% of patients had an elevated protein level, which increased to 88% of patients after 2 weeks [5]. In the same study, only 64% of GBS patients showed the characteristic albuminocytological dissociation in CSF [5]. Recently, age-specific reference values for CSF protein level were defined for children [35]. In children younger than 6 months of age, the additional value of CSF total protein determination was considered nihil, because of large physiological variation in protein levels [35].

**Nerve conduction studies**

Multiple electrophysiology criteria sets have been developed for GBS [36–38], however much debate is ongoing concerning the validity of these criteria, and on the optimal frequency of NCS for GBS subtype diagnosis [39,40]. A recent cohort study compared subtype diagnosis based on different criteria sets, and found a higher proportion of axonal cases with more recent criteria, but similar antganglioside antibody frequencies – which are considered the gold standard for subtype classification – among subtype classifications based on different criteria sets [39]. The main relevance of NCS for GBS in current clinical practice is to confirm the diagnosis, especially in atypical cases, such as paraparetic GBS, by finding either signs of demyelination or abnormalities in regions that are clinically not affected. Although nowadays classification into different subtypes has no direct therapeutic implications, this could potentially become more relevant in future management. In previous prognostic studies features of axonal degeneration were often associated with a poor prognosis, which could implicate that these patients might benefit from additional or more aggressive treatment [3]. Furthermore, the transient nature of the reversible conduction block, that has been deemed specific for AMAN [3,41], could imply an underlying antibody-mediated mechanism, for which targeted therapies could potentially be developed.

**Nerve ultrasound and MRI**

Nerve ultrasound is already a commonly used diagnostic tool in mononeuropathies and traumatic neuropathies, and its use especially in the diagnosis of chronic immune-mediated polyneuropathies is increasing [6]. Nerve ultrasound could potentially provide a useful addition to or less-invasive alternative for some currently used diagnostic techniques in GBS, especially in children. Nerve enlargement in
GBS is reported to be present 1–3 days following symptom onset, but is usually mild and segmentally distributed [6*,7*]. Proximal nerve segments and spinal nerve roots seem to be most commonly involved, but the distribution of nerve enlargement may vary with subtype [6*,7*,42]. Cervical nerve root enlargement has been described in both demyelinating and axonal forms of GBS, and in MFS [6*,7*]. Furthermore, several studies have been conducted on the diagnostic utility of contrast-enhanced spinal MRI in GBS [7*,8,9,43]. Enhancement and thickening of spinal nerve roots and cauda equina were both found in patients with typical, but also with paraparetic GBS (Fig. 1). [7*,8,9,43] MRI therefore could be helpful not only to exclude differential diagnostic abnormalities but also to indicate nerve (root) swellings that may add to the diagnosis of GBS. Additional studies in larger series of patients are however needed.

**TREATMENT**

Plasma exchange started within 4 weeks, and IVIg initiated within 2 weeks from onset of weakness, are proven effective treatments for adult patients with severe GBS [44,45]. However, GBS remains a life-threatening disorder with substantial morbidity and mortality, emphasizing the need for better treatment.

Trials that evaluated the effect of corticosteroids found no benefit compared to supportive care alone [46]. The combination of methylprednisolone with IVIg was not superior over IVIg alone, though post-hoc analysis indicated that the time to recovery seemed somewhat shorter in the IVIg plus methylprednisolone group after correction for known prognostic factors [46]. No clear benefit was observed when plasma exchange was followed by IVIg, compared to plasma exchange or IVIg alone [45]. There have been other small randomized controlled trials (RCT) with various drugs that either showed no differences between the treatment arms or were impaired by small numbers of patients [47].

In some patients, deterioration continues, even after standard treatment with plasma exchange or IVIg. These patients might potentially benefit from an additional course of treatment. There currently is a large RCT that investigates whether a second

**FIGURE 1.** Enhancement and thickening of cauda equina nerve roots on contrast-enhanced MRI. Postcontrast sagittal (left) and coronal (right) T1-weighted, fat-saturation MRIs of the lower thoracic and lumbosacral spine, performed on day 4, showing diffusely thickened cauda equina (arrowheads). CM, conus medullaris. Adapted with permission [43].
course of IVIg is of benefit when administered early in the course of disease in GBS patients with a poor prognosis. This Second IVIg Dose in GBS study (SID-GBS trial) is conducted in the Netherlands, and the results are expected early 2019 [48].

Plasma exchange and IVIg are expensive treatments that most patients in low-income countries cannot afford. This explains in part why patients in, for instance, Bangladesh show a high morbidity and mortality rate. Currently, an open study is conducted investigating the safety and feasibility of small volume plasma exchange, a low-cost alternative for plasma exchange. Results of this pilot study are soon expected [49*].

**Mild Guillain–Barré syndrome**

Most of the previously conducted RCTs are performed in adult GBS patients with severe disease. Whether patients with mild disease would benefit from treatment with IVIg or plasma exchange remains largely unknown, but some evidence suggests that the time to onset of motor recovery in mildly affected patients is reduced with two cycles of plasma exchange [45]. Treatment practice and effect of treatment in patients with mild GBS is currently being investigated in the International GBS Outcome Study, a multicenter prospective cohort study on GBS [50].

**Children**

Trials in children are sparse, but limited evidence suggests a benefit of IVIg in hastening recovery over supportive care alone [44].

**Pain**

Pain is a frequently reported symptom, and occurs in the full spectrum of GBS, and at all stages of disease [3,4]. In a subgroup of patients, pain precedes the onset of weakness, which may induce diagnostic delay, particularly in children [3,4]. Defining the appropriate management for pain in GBS is complicated, because of the varying types of pain and unknown underlying pathogenic mechanisms [3,4]. In the acute phase of GBS, significant reductions in pain scores and reduced analgesic consumption were reported for gabapentin and carbamazepine [51]. No effect on the frequency of reported pain or pain severity was observed for treatment with methylprednisolone [51]. Larger, high-quality trials are needed to evaluate safety and efficacy of therapeutic interventions for pain in GBS, both in the acute and recovery phase of disease.

**Novel therapies**

Much effort has been made in the development of therapeutics that prevent the complement-dependent neuronal damage underlying GBS [13*,14]. Two randomized, double blind, placebo-controlled phase 2 trials have evaluated the safety and efficacy of eculizumab – a complement factor S inhibitor – in GBS (Fig. 2). In the Inhibition of Complement Activation in GBS study, patients were randomized to receive IVIg with eculizumab or placebo. The small patient number precluded conclusions on efficacy, but eculizumab was deemed safe and well tolerated [15*]. The Japanese Eculizumab Trial for GBS used the same study protocol, and randomized 23 patients to IVIg with eculizumab, and 12 patients to IVIg with placebo. The predefined response rate threshold for the eculizumab group was not reached, but a larger proportion of patients in the eculizumab group were able to run at 24 weeks (74%), than in the placebo group (18%). In most patients, eculizumab was well tolerated, although causality with two serious adverse events could not be excluded [16**]. These studies implicate that eculizumab seems safe and well tolerated, and might potentially improve outcome in GBS as add-on treatment to IVIg, but larger trials are required. Another complement inhibitor that was shown effective in mouse models of AMAN and MFS is an anti-complement factor 1 (C1)q antibody (Fig. 2) [13*]. Currently, a phase 1 clinical trial to assess safety and tolerability of anti-C1q antibody (ANX005) in healthy volunteers is being conducted [52].

Another potentially promising therapeutic agent is the IgG-degrading enzyme that is secreted by *Streptococcus pyogenes* (IdeS). The enzyme cleaves IgG-molecules into the antigen-binding fragment - F(ab')2 - and Fc-portion, and is therefore expected to be effective in GBS through the cleavage of pathogenic antibodies (Fig. 2) [53]. A phase 2 trial for IdeS is planned in Europe [54*]. Furthermore, reports of in vitro and animal studies and case reports on the efficacy of biological drugs in GBS show promising results, but clinical trials are needed to extent these findings [55*].

**PROGNOSIS AND OUTCOME**

**Relapses of Guillain–Barré syndrome**

GBS is usually a monophasic disease, but secondary deteriorations after initial stabilization or improvement occur in 5–10% of treated GBS patients [3,56*]. These “treatment-related fluctuations” are thought to result from a transient treatment effect in patients with a prolonged disease activity. Some patients may have two or more deteriorations, and are
eventually diagnosed with acute-onset chronic inflammatory demyelinating polyneuropathy (A-CIDP), or have a recurrent episode of GBS. The differentiation between GBS with treatment-related fluctuation, A-CIDP, and recurrent GBS is important, especially because A-CIDP might require maintenance treatment or a switch from IVIg to corticosteroids. A-CIDP should specifically be considered in patients with three or more subsequent deteriorations, or when the first deterioration occurs more than 8 weeks after the onset of weakness [3,56]. GBS recurrences are reported in 2–7% of GBS cases, and seem to occur more frequently in younger patients, patients with a mild disease course, and MFS [57–59]. Another study found more recurrences in patients with AIDP than in patients with axonal subtypes [59].

**Miller Fisher syndrome**
Outcome in typical MFS is usually considered to be favorable, with high likelihood of complete recovery, even with a conservative approach [60]. However, a substantial proportion of patients with MFS develop additional limb weakness (±25–40%), bulbar weakness (40%) or autonomic disturbances (10%) during the course of disease [61–63]. Early predictive factors for progression of MFS to MFS–GBS overlap syndromes have not yet been identified, but progression of MFS after 1 week from symptom onset is rare [62,63]. Therefore, close monitoring of MFS patients for at least 1 week is advised [60,63].

**Clinical predictors**
Despite standard treatment, about 25% of patients with GBS require mechanical ventilation [3]. In a recent meta-analysis, an increased risk of intubation was found in patients with a shorter duration from symptom onset to hospital admission, neck, or bulbar weakness, and more severe muscle weakness at admission [64**]. One study found an association between coexisting infectious illness at admission,
specifically cytomegalovirus and herpes simplex virus infections, and the need for mechanical ventilation [65]. The Erasmus GBS Respiratory Insufficiency Score (EGRIS) is a prognostic model that predicts the probability of respiratory failure within the first week of admission in individual patients with GBS, based on the time from onset of weakness to hospital admission, presence of facial and/or bulbar weakness at admission, and the MRC sum score at admission (Fig. 3) [18,64]. Mechanical ventilation appears to be a negative predictive factor for long-term outcome in GBS, and is often accompanied by both local and systemic complications [19*,66]. Several factors have been associated with prolonged mechanical ventilation, for example, the inability to lift the upper arms from the bed, axonal damage, and unresponsive nerves on NCS. Presence of these features could guide the decision for early tracheostomy in individual patients, to prevent tracheal or vocal cord damage [19*]. Poor outcome in GBS is often defined as the inability to walk unaided during follow up. The modified Erasmus GBS Outcome Score (mEGOS) is a clinical scoring system that predicts the probability of being unable to walk independently during the first six months follow up, based on age, preceding diarrhea, and MRC sum score (Fig. 4) [17]. Prognostic models can be applied in therapeutic trials to identify patients that might benefit from additional treatment, as has been done in the SID-GBS trial. The EGRIS and mEGOS were originally based on a cohort of Dutch GBS patients, and recently also showed good performance in a Japanese cohort [67]. Additional validation studies in other countries are required to assess the generalizability of these models.

**Biomarkers**

Serum albumin was recently proposed as a new and easily accessible biomarker for GBS [68*]. Low pre and posttreatment serum albumin levels were associated with respiratory failure, and low posttreatment levels were associated with a more severe disease course and poorer outcome at 6 months. The addition of serum albumin to the EGRIS and mEGOS models resulted in a better predictive ability, indicating that biomarkers may improve the accuracy of existing clinical prediction models [68*,69].
CONCLUSION AND FUTURE PERSPECTIVES

Since the first description of GBS over a century ago, knowledge on the pathophysiology and diversity of the clinical syndrome has greatly evolved, and treatment with IVIg or plasma exchange has been introduced [10]. The validity of existing electrophysiology criteria for GBS is under debate, and research is being performed on the diagnostic utility of nerve ultrasound and MRI in the diagnosis of GBS. A new international guideline for the management of GBS is currently being developed by the European Academy of Neurology and the Peripheral Nerve Society. There is increasing evidence that complement activation plays a critical role in the pathophysiology of GBS. The first results of small trials with eculizumab are promising, but need to be confirmed in larger studies. Additional trials with other inhibitors of the complement cascade or with drugs that interfere with pathogenic or complement fixing antibodies are indicated. In the meantime, the results of the SID-GBS RCT, evaluating the effect of a second course of IVIg in GBS patients with a poor prognosis, are eagerly awaited. Current prognostic models for GBS are a required condition to personalize treatment. An opportunity to validate these models in an international population of patients and to discover new clinical and biological predictors of outcome will come from the International GBS Outcome Study, world’s largest prospective study on GBS [50].

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Conflicts of interest  
Funding sources (P.A.D. and B.C.J.) (for studies that are referred to in this review): Annexon, Baxter, CSL Behring, GBS-CIDP Foundation International, Grifols, Hansa, Horizon 2020, Kedrion, Princes Beatrix Spierfonds, Sanquin Blood Supply. P.A.D is PI of the RCT investigating the effect of methylnprednisolone in GBS (methylprednisolone/IVIg RCT in GBS) and the RCT investigating the effect of a second dose IVIg in GBS (SID-GBS study). A.Y.D. has no conflicts of interest.

REFERENCES AND RECOMMENDED READING

Papers of particular interest, published within the annual period of review, have been highlighted as:  
■ of special interest  
□ of outstanding interest


A detailed description is provided of the key diagnostic features included in the Brighton criteria for a large cohort of Dutch GBS patients. This is the first study to describe the association between CSF total protein level and timing of lumbar puncture.


This article gives an overview of the diagnostic role of nerve ultrasound in management of polyneuropathies. A description is provided of sonographic parameters that can be evaluated, and abnormalities that can be found in different inherited and acquired polyneuropathies.


This article summarizes the current evidence for the early and prominent role of proximal nerve (root) involvement in the pathogenesis of GBS and the implications for clinical practice.


This review describes the progress that has been made in the past century in the pathological and clinical characterization of GBS. Evidence from clinico-pathological studies and animal studies has led to a paradigm shift from GBS as an immune-mediated demyelinating disorder with (secondary) axonal damage in severe cases, to GBS as a heterogenic disorder comprising different clinical and electrophysiological entities, and primary antibody-mediated, complement-dependent axonal injury.


This case–control study provides the first evidence for an association between ZIKV infection and GBS, following the ZIKV outbreak in French Polynesia.


Evidence from this study supports an association between ZIKV infection and GBS, and also illustrates the global spread of ZIKV following the first large outbreak in French Polynesia.


This study demonstrates the neuroprotective effect of C1q inhibition in AMAN and MFS mouse models, a promising new therapeutic target for GBS in humans.


This is the first phase 2 clinical trial to evaluate the safety and efficacy of eculizumab—a humanized monoclonal antibody to complement factor C5—in the treatment of GBS. Eculizumab seemed safe and well tolerated. A detailed description of the study protocol is also provided. A similar protocol was used for Japanese Eculizumab Trial for GBS.


This phase 2 RCT provides supporting evidence for the safety and tolerability of eculizumab in the treatment of GBS, and presents some promising results on the efficacy of eculizumab as add-on treatment to IVlg.


Long-term mechanical ventilation is often accompanied by complications. Local damage to the trachea and vocal cords can be prevented by early consideration of tracheostomy. This article provides clinical and electrophysiological characteristics of patients with GBS that are mechanically ventilated, that can be used to predict the probability of long-term mechanical ventilation, and could therefore give the decision for early tracheostomy in clinical practice.


This retrospective cohort study presents supporting evidence for the association between HEV infection and GBS. It provides some first guidelines for testing of infectious agents in GBS, notifying the possibility of cross-reactivity of HEV with cytomegalovirus and Epstein-Barr virus.


This case–control study firstly describes the association between M. pneumoniae infection and pediatric GBS. A correlation was found between anti-M. pneumoniae antibodies and anti-GaC antibodies. Cross-reactivity was observed between anti-GaC antibodies and different strains of M. pneumoniae, suggesting a possible role for anti-GaC antibodies in the pathophysiology of GBS.


This review gives an overview of the epidemiology of ZIKV infection and associated neurological syndromes, and provides practical guidelines for diagnosing ZIKV infections in travelers returning from ZIKV endemic regions.


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33. This study provides a detailed description of the key presenting and diagnostic features of GBS in children, according to the Brighton criteria.


35. This retrospective study describes the differences in clinical presentation, disease severity, treatment, and outcome between children and adults with GBS, in a large Chinese cohort.


40. This study compared GBS subtype diagnosis when using traditional (Ho, Hadden and new (Rajabally) NCS criteria and showed that the classification into subtypes is highly dependent on the NCS criteria set that is being used.


42. This study evaluated the accuracy of different electrophysiology criteria sets for GBS with single NCS. Classifications based on these different criteria sets were compared to a reference electrodiagnosis that was based on serial NCS and antganglioside antibody testing. A novel statistical method was introduced (sparse linear discriminant analysis) to classify patients into axonal and demyelinating subtypes.


55. This review provides an overview of the novel therapeutic agents that have been developed for GBS, and the upcoming therapeutic trials. Of special interest is the planned trial with ldes.


62. This systematic review and meta-analysis provides an overview of the individual predictors and clinical prediction rules for respiratory insufficiency in GBS.


67. Current prognostic models for GBS are mainly based on clinical parameters. This article provides evidence for serum albumin level as a potential and easily accessible biomarker for the severity and outcome of GBS in IV Ig treated GBS patients.
