doi:10.1093/brain/aww247 BRAIN 2016: 139; 3041–3047 | 3041

BRAIN
A JOURNAL OF NEUROLOGY

DORSAL COLUMN

Grey Matter

# Guillain-Barré syndrome in the 100 years since its description by Guillain, Barré and Strohl

**Richard A. C. Hughes,[1] David R. Cornblath[2] and Hugh J. Willison[3]**

1 University College London, Institute of Neurology, London, UK
2 The Johns Hopkins University, Meyer 6-181a, 601 North Wolfe St, Baltimore, MD 21287-7681, USA
3 Institute of Infection, Immunity and Inflammation, College of Medical, Veterinary and Life Sciences, Glasgow Biomedical Research Centre 120 University Place Glasgow G12 8TA, UK

**Keywords:** Guillain-Barré syndrome; history; pathology; Zika virus; treatment

**Abbreviations:** AIDP = acute inflammatory demyelinating polyradiculoneuropathy; AMAN = acute motor axonal neuropathy; GBS = Guillain-Barré syndrome

## The first descriptions

Landry's 1859 description of 10 cases of acute ascending paralysis fitted well with the modern concept of Guillain-Barré syndrome (GBS) but necessarily lacked the defining features of tendon areflexia and CSF albuminocytological dissocation (Landry, 1859). Westphal and Erb described examination of the patellar tendon reflex in 1875 and examination of this and other reflexes rapidly entered regular neurological practice (Erb, 1875; Westphal, 1875; Boes, 2014). Quincke (1891) introduced lumbar puncture for the management of hydrocephalus in 1891. These discoveries set the stage for the seminal paper of Guillain, Barré and Strohl in 1916 (Guillain *et al.*, 1916). A meeting of the Inflammatory Neuropathy Consortium of the Peripheral Nerve Society in Glasgow from 21–24 June 2016 (www.pnsociety.com/inflammatory-neuropathy-consortium) celebrated its centenary. A 63-chapter companion book records the centennial reflections of the speakers and others (Willison and Goodfellow, 2016).

## The 1916 description by Guillain, Barré and Strohl

Guillain, G., Barré, J.A., & Strohl, A. 1916. Sur un syndrome de radiculo-névrite avec hyperalbuminose du liquide céphalo-rachidien sans réaction cellulaire. Remarques sur les caractères cliniques et graphiques des réflexes tendineux. Bull Soc Méd Hôp Paris, 40, 1462–70

On 13 October 1916, during the battle of the Somme, members of the Société de Neurologie serving in the French Army held a meeting where Guillain, Barré and Strohl described two soldiers with weakness of the limbs.

> 'The first soldier D... of the hussars, 25 years old, arrived at the neurological centre of the Sixth Army because of motor disturbances of the lower and upper limbs on the 20th August 1916. The illness began on 25th July with tingling of the feet and weakness of the lower limbs making him stop walking after 200 to 300 metres. The tingling then spread to the upper limbs and lower part of the face during the following days and he developed weakness in the upper limbs.'

Five days later, examination showed severe generalized weakness more pronounced distally and mild impairment of touch, pain and temperature sensation on his hands. He could only walk a few steps and his gait was unstable. The second soldier D...of the infantry, 35 years old, arrived at the same army centre on 5 September 1916 with leg weakness. It began on 28 August after a 15 km walk and spread from his legs to his arms. The next morning he fell over when he shouldered his backpack and could not get up. Examination showed that

> 'with effort he could make small extension and flexion movements of the toes, knees and hips. He had the same difficulty

Received July 25, 2016. Revised September 8, 2016. Accepted September 9, 2016

with the upper limbs, especially distally. His head was mostly turned to the left and he had difficulty turning it to the right. He could open and close his mouth but slowly and incompletely'.

Some of these findings are difficult to explain on the basis of a diagnosis of acute neuropathy, especially when we read that the reflexes were difficult to obtain because of '*l'hypertonie musculaire*'. The signs reported suggest that more than peripheral nerve disease was responsible. However, a centenary is not the time to be challenging a diagnosis. Like the first soldier, the second had distal tingling and slight reduction of sensation. Importantly, in both cases the tendon reflexes were absent and the CSF protein concentrations were increased despite a normal cell count. The first soldier could walk for an hour by the time he was discharged 30 days after being seen. The second had improved before being sent for convalescence after 25 days.

Guillain-Barré syndrome did not gain immediate acceptance into the canon and the following year Gordon Holmes was continuing to use Osler's term 'Acute Febrile Polyneuritis' (Holmes, 1917) to describe 'about twelve' soldiers with an illness indistinguishable to the modern reader from GBS. Although he used the term febrile, most of the men were seen by Holmes when the disease was well established and they were no longer febrile. The timing of the febrile illness in relation to the onset of weakness is not clearly described except in one in whom the onset occurred 'a short time' after relapsing trench fever and another who had had diarrhoea and vomiting 'within the previous few weeks'. Two of Holmes' patients died whereas Guillain continued to insist that the course of GBS was benign and death rare, although in his last word on the subject he conceded that it did not confer immortality (Guillain, 1953).

# Pathology

Holmes found that the sciatic nerves of the fatal cases 'contained some fibres in the early stage of degeneration, their myelin sheaths being broken up into chains of spherical or oval globules, while the calibre of other fibres was irregular and their staining unequal'. During World War II, Haymaker and Kernohan in the US Army Institute of Pathology collected material from 50 autopsies from all theatres of war around the world (Haymaker and Kernohan, 1949). They found that the pathology was confined to the peripheral nerves and, in their limited material, affected in particular the point at which the ventral and dorsal spinal roots fuse. They considered that the earliest change was oedema, followed by swelling and irregularity of the myelin sheaths and axis cylinders and only later lymphocyte and phagocyte infiltration. However, Krücke soon described seven personal cases in which cellular, predominantly lymphocytic, infiltration was the first abnormality, present from the first days of the disease (Krücke, 1955). By this time autoallergy had become a popular cause of disease and experimental encephalitis had been produced by injecting monkeys with rabbit brain. Waksman and Adams (1955, 1956) injected peripheral nerve tissue with Freund's adjuvant into laboratory animals producing experimental allergic neuritis (EAN) with extensive lymphocytic and histiocytic infiltration of the peripheral nerves, spinal roots and dorsal root ganglia. From the same institution, the Massachusetts General Hospital, Asbury, Arnason and Adams published a collection of 19 autopsies which showed very similar changes associated with demyelination (Asbury *et al.*, 1969). The histological appearances led to GBS being regarded as synonymous with acute inflammatory demyelinating polyradiculoneuropathy (AIDP) (Arnason, 1984). Electron microscope studies in both EAN and in GBS biopsies subsequently showed that demyelination begins with macrophage invasion, digestion and stripping of intact myelin sheaths (Lampert, 1969; Prineas 1972, 1981). This histological similarity led to extensive studies showing that EAN is driven by T cell responses against myelin proteins P2, P0 or PMP22 and potentially exacerbated by antibodies to glycolipids (Kadlubowski and Hughes, 1979; Linington *et al.*, 1984, 1992; Milner *et al.*, 1987; Hahn *et al.*, 1993; Gabriel *et al.*, 1998). Furthermore, certain mouse strains with defective immunoregulatory genes spontaneously develop autoimmune neuropathy due to T cells reacting against myelin P0 protein (Salomon *et al.*, 2001; Louvet *et al.*, 2009; Su *et al.*, 2012; Meyer zu Horste *et al.*, 2014). These observations showed that T cell responses to myelin proteins can induce inflammatory neuropathy. Nevertheless, attempts to identify antibody or T cell responses to the same antigens in human neuropathies have only rarely been successful and then only in a few patients without any detected relationship to clinical features (Makowska *et al.*, 2008).

## Acute motor axonal neuropathy

In 1986, Feasby and colleagues reported five patients, including one autopsy study, with a form of GBS in which the predominant abnormality was axonal degeneration (Feasby *et al.*, 1986). Shortly after, McKhann *et al.* (1991, 1993) investigated an epidemic of GBS occurring in the summer months in children in Northern China. The neuropathy resembled the conventional form of GBS clinically but was usually predominantly motor and the electrophysiological findings were strikingly different with reduced compound muscle action potentials without conduction slowing implicating an axonal pathology. Subsequent histological studies of autopsy material supported this conclusion and validated the concept of acute motor axonal neuropathy (AMAN) (Griffin *et al.*, 1995). Rather than endoneurial infiltration of T cells and penetration of the myelin sheaths by macrophages to produce demyelination as in AIDP, in these autopsied cases there was invasion of macrophages into the periaxonal space at the paranodes followed by degeneration of the axons while the myelin sheaths remained intact (Griffin *et al.*, 1996). In

some particularly severe cases the sensory axons were affected as well, producing acute motor and sensory axonal neuropathy (AMSAN). Investigation of the cause of these conditions has been much more successful than that of AIDP. Deposits of IgG and C3d on the axolemma of the affected axons in AMAN implicated an antibody-mediated mechanism (Hafer-Macko *et al.*, 1996). Antibodies to gangliosides were already known to occur in GBS (Ilyas *et al.*, 1988) and antibodies to ganglioside GM1, GD1a and GalNAc-GD1a were found to be particularly common in AMAN. Yuki and colleagues produced a convincing model replicating the electrophysiological and histological appearances of AMAN by immunizing rabbits with ganglioside GM1 (Susuki *et al.*, 2003). Willison produced a more refined mouse model in which passively transferred monoclonal antibodies to GD1a destroyed the motor nerve terminals (Goodfellow *et al.*, 2005; McGonigal *et al.*, 2010; Willison, 2012). Many of the patients with AMAN in the studies in China had had *Campylobacter jejuni* infection, which was soon recognized as the commonest precipitant of GBS throughout the world. Strains of *Campylobacter* associated with GBS carry epitopes in the lipooligosaccharide in their cell walls, which antibodies to ganglioside GM1 or GD1a recognize (Yuki *et al.*, 1993). A likely cause of AMAN is that a bacterium carrying a ganglioside-like epitope in its cell walls triggers an antibody response that cross-reacts with axolemmal antigens in immunogenetically susceptible subjects. The hypothesis is convincing but lacks an explanation for the breakdown of the blood–nerve barrier to allow the antibodies access to the endoneurium. In very distal intramuscular nerves and in spinal roots, this may not represent a significant barrier.

## Neurophysiology

As sampling peripheral nerve tissue to investigate the underlying pathology is invasive and site-limited, neurophysiological testing is crucially important in distinguishing between the various forms of GBS. Early papers reported markedly slowed nerve conduction velocities and delayed distal motor nerve latencies consistent with demyelination (Bannister and Sears, 1962; Wiederholt *et al.*, 1964; McLeod, 1981). The description of an axonal form of the disease by Feasby and colleagues and the cases of AMAN in China led to attempts to separate the cases of GBS into two groups from the electrophysiological features (Hadden *et al.*, 1998). These attempts have been complicated by the changes that occur as the disease progresses, so that patients who were classified as having demyelinating features at onset are reclassified as axonal 2 weeks later and vice versa. Part of the confusion arises because transient failure of impulse conduction, from whatever cause and at whatever site along the nerve, can either be followed by rapid recovery or lead to distal axonal degeneration. This can lead to confusion when one tries to pigeon hole these rapidly changing findings into either ‘axonal’ or ‘demyelinating’, terms usually reserved for chronic neuropathies. The confusion has led to a call for serial studies to enable a more accurate classification (Uncini and Kuwabara, 2012).

## Other syndromes

In addition to the typical generalized polyneuropathy seen in AIDP and AMAN or AMSAN, regional variants of GBS have become recognized and some have associations with antibodies to particular gangliosides (Table 1). In the best known of these, the Fisher syndrome of ophthalmoplegia, areflexia and ataxia, named after Charles Miller Fisher (Fisher, 1956), there is convincing evidence for the role of antibodies. Ninety per cent of patients with Fisher syndrome have antibodies to ganglioside GQ1b (Chiba *et al.*, 1992). Ganglioside GQ1b is enriched in human ocular motor nerves and at mouse motor nerve terminals. Application of monoclonal anti-GQ1b antibody and complement to mouse motor nerve terminals caused lysis of both the terminal axon and the perisynaptic Schwann cell (Halstead *et al.*, 2004). As pure Fisher syndrome is relatively benign, post-mortem studies are not available and biopsies of affected parts of the peripheral nervous system are impractical, so that the underlying pathology has not been extensively studied. In one pathological case report, sural biopsy did show lengthening of nodes of Ranvier, myelin splitting and macrophage internodal axonal invasion without any features of segmental demyelination (Miller *et al.*, 2014). GQ1b has been localized by immunohistology with anti-GQ1b antibodies to both paranodal Schwann cell membranes and motor nerve terminals of human extraocular nerves (Chiba *et al.*, 1997; Liu *et al.*, 2009), indicating that both sites may be vulnerable to immune attack. In sensory nerve electrophysiology studies, sensory action potentials have been shown to diminish in amplitude during the acute phase of the illness, and then recover, suggesting reversible conduction failure (Guiloff, 1977; Umapathi *et al.*, 2012). Ophthalmoplegia does occur in GBS and patients who present with ophthalmoplegia, areflexia and ataxia may go on to develop generalized limb weakness, resulting in a GBS-Fisher overlap syndrome. Furthermore instead of ascending paralysis or generalized weakness occasional patients have descending weakness affecting the face, bulbar muscles and upper limbs. Many formes frustes and related disorders including Bickerstaff’s encephalitis occur (Al-Din *et al.*, 1982; Odaka *et al.*, 2001; Ito *et al.*, 2008).

The course of GBS is usually acute and monophasic but a small per cent have recurrent disease and in up to 16% of cases of chronic inflammatory demyelination polyradiculoneuropathy (CIDP) the onset is acute, establishing a spectrum between that disease and AIDP (McCombe *et al.*, 1987; Dionne *et al.*, 2010). The pathogenesis of CIDP is not well understood. Like GBS it is probably heterogeneous. IgG4 antibodies to paranodal proteins contactin and neurofascin 155 occur in a very small percentage of

**Table 1 Guillain-Barré syndrome subtypes, related disorders and associated antiganglioside antibodies**

| Syndrome | Associated antiganglioside antibodies |
|---|---|
| AIDP | None |
| AMSAN | GM1, GM1b, GD1a |
| AMAN | GM1, GM1b, GD1a, GalNac-GD1a |
| Acute sensory neuronopathy | GD1b |
| Fisher syndrome | GQ1b, GT1a |
| Fisher/GBS overlap syndrome | GQ1b, GM1, GM1b, GD1a, GalNac-GD1a |
| Cervico-brachial-oropharyngeal syndrome | GT1a |

AMSAN = acute motor and sensory axonal neuropathy.

patients with CIDP and may be pathogenic in this small subgroup (Mathey *et al*., 2015).

## Diagnosis

A committee of the American National Institute of Neurological and Communicative Disorders and Stroke proposed diagnostic criteria for research that included clinical features of progressive limb weakness and loss of tendon reflexes with supportive CSF and electrodiagnostic features (Asbury *et al*., 1978). These worked well in clinical practice (Asbury and Cornblath, 1990), but the acceptance of variants and formes frustes complicated the application of such criteria. More recently the Brighton organization published more explicit consensus diagnostic criteria of both GBS and Fisher syndrome for use in epidemiological studies (Sejvar *et al*., 2011b). These include clinical, neurophysiological and CSF criteria and exclusion of other causes. The possibility of only mild neurophysiological changes and frequently normal CSF, especially in the first week of the illness, complicate the application of these criteria in practice. In a retrospective study of 335 adult Northern European patients collected in clinical trials and observational studies only 61% fulfilled all criteria, but 94% fulfilled the clinical and either neurophysiological or CSF criteria (Fokke *et al*., 2014). In the absence of a diagnostic biomarker, diagnosis will continue to depend on recognition of the characteristic clinical picture and exclusion of other causes.

## Epidemiology

GBS is usually an uncommon sporadic disease. In a systematic review of studies from North America and Europe, the crude incidence of GBS ranged from 0.81 to 1.89 cases per 100 000 person–years (Sejvar *et al*., 2011a). The incidence rises with increasing age, being 0.62 cases per 100 000 person–years among 0 to 9 year olds and 2.66 cases per 100 000 person–years among 80 to 89 year olds. It is more common in males than females, the relative risk being 1.78 (95% confidence interval, 1.36–2.33) times greater in males. The reasons for the age and sex distribution are unknown and are not typical of autoimmune disease.

In 1976 there was an epidemic of GBS following the swine flu vaccination programme in the USA in which the eventual conclusion was that the rate of attributable cases had been between 0.49 and 0.59 cases per 100 000 adult vaccinees over the 6 to 8 week period after the vaccine (Langmuir *et al*., 1984). Since then the occurrence of GBS has become a bellwether of the safety of vaccination programmes. Subsequent influenza vaccines have either not been associated with GBS or the attributable risk has only been ~0.1 additional GBS cases above expected per 100 000 vaccinees. There have been occasional small epidemics of GBS associated with infectious illnesses but the most striking epidemics of GBS so far encountered have been those associated with Zika virus both in French Polynesia in 2013 and 2014 (Cao-Lormeau *et al*., 2016) and South America in 2015 and 2016 (Dos Santos *et al*., 2016; Pardo, personal communication). The 42 incident cases from French Polynesia were significantly more likely to have antibodies against Zika virus than contemporary controls admitted to hospital with a non-febrile illness. The neurophysiological features were interpreted to represent AMAN, although review of the published data suggests that many of these cases were in fact AIDP-based on the presence of prolonged distal motor latencies. The AIDP phenotype is similar to the experience with Zika virus-associated GBS in Colombia (Pardo, personal communication). Although antibodies to glycolipids were present in some patients from French Polynesia, there were none of the antibodies to ganglioside GM1 and GD1a previously associated with *Campylobacter*-associated AMAN, suggesting pathophysiological distinctions between post-Zika GBS in French Polynesia and typical AMAN.

Besides *Campylobacter* and Zika virus, the other principal infections established as occurring before GBS more often than chance are cytomegalovirus, *Mycoplasma pneumoniae*, Epstein-Barr virus, *Haemophilus influenzae* and hepatitis E (Willison *et al*., 2016). There is a long list of case reports and small case series implicating other agents of which herpes zoster and HIV are particularly plausible candidates. The fundamental question remains whether these all produce the disease by eliciting an antibody response against an antigen in the infective agent cell wall, as in the likely *Campylobacter* mechanism, or in the host membrane that a virus may collect in its envelope during budding, or in some other way.

The ongoing International Guillain-Barré syndrome Outcome Study (IGOS) has collected more than 1300 of its target 1500 patients from centres in 18 countries in North America, Europe and Australasia. The interim results confirm that the clinical picture is different in different parts of the world. The usual sensory and motor form of the disease is the commonest in most countries but in Bangladesh a pure motor form is the most common (van den Berg for the IGOS consortium, 2016). As the study

continues it should be possible to correlate this observation with neurophysiological subtypes, knowledge of the antecedent events and serum biomarkers and so shed further light on the pathogenesis.

## Clinical course and treatment

The usual course of the disease is progression continuing for 1 to 28 days, a plateau phase of several days or even weeks and then gradual recovery, sometimes complete but often not. Increasingly sophisticated prognostic scores have been derived from natural history studies or data from patients participating in treatment trials. One of these allows prediction of the ability to walk after 6 months from the age, presence of a preceding diarrhoeal illness and a GBS disability grade score: older age, preceding diarrhoea and worse disability all predict a worse prognosis (van Koningsveld *et al.*, 2007). Another allows prediction of the need for ventilation from the time to hospital admission, presence of facial or bulbar weakness and strength measured with the Medical Research Council sum score (the sum of the scores of 12 muscle groups) (Walgaard *et al.*, 2010).

Guillain, Barré and Strohl treated their first patient with rest, massage and strychnine. Since then, supportive care, occupational and physical therapy, and artificial ventilation have been the mainstays of treatment. Plasma exchange or intravenous immunoglobulin, but not corticosteroids, have been shown to hasten recovery (Hughes *et al.*, 2007). Despite these treatments improvement is often slow and incomplete, and patients continue to suffer from pain and fatigue. In the Netherlands only ~3% of patients with GBS enrolled in clinical trials or observational studies between 1986 and 2008 died, but the mortality has been closer to 10% in countries without excellent intensive care facilities (van den Berg *et al.*, 2013). In the mouse models of AMAN and Fisher syndrome, complement fixing antibodies and complement fixation are critical for pathogenesis, and complement blockade is highly effective as treatment (Willison *et al.*, 2008). It is greatly hoped that ongoing trials of complement blockade with the complement blocking drug eculizumab added to the usual intravenous immunoglobulin regime will improve the outcome from GBS.

# Funding

No funding was received towards this work.

# References

Al-Din AN, Anderson M, Bickerstaff ER, Harvey I. Brainstem encephalitis and the syndrome of Miller-Fisher: a clinical study. Brain 1982; 105: 481–95.

Arnason BGW. Acute inflammatory demyelinating polyradiculoneuropathies. In: Dyck PJ, Thomas PK, Lambert EH, Bunge R, editors. Peripheral neuropathy. Philadelphia: Saunders, W.B.; 1984. p. 2050–100.

Asbury AK, Arnason BG, Adams RD. The inflammatory lesion in idiopathic polyneuritis. Its role in pathogenesis. Medicine 1969; 48: 173–215.

Asbury AK, Arnason BGW, Karp HR, McFarlin DF. Criteria for diagnosis of Guillain-Barré syndrome. Ann Neurol 1978; 3: 565–6.

Asbury AK, Cornblath DR. Assessment of current diagnostic criteria for Guillain-Barré syndrome. Ann Neurol 1990; 27 (Supp l): S21–24.

Bannister RG, Sears TA. The changes in nerve conduction in acute idiopathic polyneuritis. J Neurol Neurosurg Psychiatry 1962; 25: 321–8.

Boes CJ. The history of examination of reflexes. J Neurol 2014; 261: 2264–74.

Cao-Lormeau VM, Blake A, Mons S, Lastère S, Roche C, Vanhomwegen J, et al. Guillain-Barré syndrome outbreak associated with Zika virus infection in French polynesia: a case-control study. Lancet 2016; 387: 1531–9.

Chiba A, Kusunoki S, Obata H, Machinami R, Kanazawa I. Ganglioside composition of the human cranial nerves, with special reference to pathophysiology of Miller Fisher syndrome. Brain Res 1997; 745: 32–6.

Chiba A, Kusunoki S, Shimizu T, Kanazawa I. Serum IgG antibody to ganglioside GQ1b is a possible marker of Miller Fisher syndrome. Ann Neurol 1992; 31: 677–9.

Dionne A, Nicolle MW, Hahn AF. Clinical and electrophysiological parameters distinguishing acute-onset chronic inflammatory demyelinating polyneuropathy from acute inflammatory demyelinating polyneuropathy. Muscle Nerve 2010; 41: 202–7.

Dos Santos T, Rodriguez A, Almiron M, Sanhueza A, Ramon P, de Oliveira WK, et al. Zika Virus and the Guillain-Barré syndrome - case series from seven countries. N Engl J Med 2016. doi: 10.1056/NEJMc1609015, in press.

Erb W. Ueber Sehnenreflexe bei Gesunden und bei Rückenmarkskranken. Arch Psychiatr Nervenkr 1875; 5: 792–802.

Feasby TE, Gilbert JJ, Brown WF, Bolton CF, Hahn AF, Koopman WF, et al. An acute axonal form of Guillain-Barré polyneuropathy. Brain 1986; 109: 1115–26.

Fisher M. An unusual variant of acute idiopathic polyneuritis (syndrome of ophthalmoplegia, ataxia and areflexia). N Engl J Med 1956; 255: 57–65.

Fokke C, van den Berg B, Drenthen J, Walgaard C, van Doorn PA, Jacobs BC. Diagnosis of Guillain-Barré syndrome and validation of Brighton criteria. Brain 2014; 137: 33–43.

Gabriel CM, Hughes RAC, Moore SE, Smith KJ, Walsh FS. Induction of experimental neuritis with peripheral myelin protein 22. Brain 1998; 121: 1895–902.

Goodfellow JA, Bowes T, Sheikh K, Odaka M, Halstead SK, Humphreys PD, et al. Overexpression of GD1a ganglioside sensitizes motor nerve terminals to anti-GD1a antibody-mediated injury in a model of acute motor axonal neuropathy. J Neurosci 2005; 25: 1620–8.

Griffin JW, Li CY, Ho TW, Xue P, Macko C, Gao CY, et al. Guillain-Barré syndrome in northern China. The spectrum of neuropathological changes in clinically defined cases. Brain 1995; 118: 577–95.

Griffin JW, Li CY, Macko C, Ho TW, Hsieh ST, Xue P, et al. Early nodal changes in the acute motor axonal neuropathy pattern of the Guillain-Barré syndrome. J Neurocytol 1996; 25: 33–51.

Guillain G. Considerations sur le syndrome de Guillain et Barré. Ann de Médecine 1953; 54: 81–149.

Guillain G, Barré JA, Strohl A. Sur un syndrome de radiculo-névrite avec hyperalbuminose du liquide céphalo-rachidien sans réaction cellulaire. Remarques sur les caractéres cliniques et graphiques des réflexes tendineux. Bull Soc Méd Hôp Paris 1916; 40: 1462–70.

Guiloff RJ. Peripheral nerve conduction in Miller Fisher syndrome. J Neurol Neurosurg Psychiatry 1977; 40: 801–7.

Hadden RDM, Cornblath DR, Hughes RAC, Zielasek J, Hartung HP, Toyka KV, et al. Electrophysiological classification of Guillain-Barré

syndrome: clinical associations and outcome. Ann Neurol 1998; 44: 780–8.
Hafer-Macko C, Hsieh ST, Li CY, Ho TW, Sheikh K, Cornblath DR, et al. Acute motor axonal neuropathy: an antibody-mediated attack on axolemma. Ann Neurol 1996; 40: 635–44.
Hahn AF, Feasby TE, Wilkie L, Lovgren D. Antigalactocerebroside antibody increases demyelination in adoptive transfer experimental allergic neuritis. Muscle Nerve 1993; 16: 1174–80.
Halstead SK, O'Hanlon GM, Humphreys PD, Morrison DB, Morgan BP, Todd AJ, et al. Anti-disialoside antibodies kill perisynaptic Schwann cells and damage motor nerve terminals via membrane attack complex in a murine model of neuropathy. Brain 2004; 127: 2109–23.
Haymaker W, Kernohan JW. The Landry-Guillain-Barré syndrome: a clinicopathologic report of fifty fatal cases and a critique of the literature. Medicine 1949; 28: 59–141.
Holmes G. Acute febrile polyneuritis. Brit Med J 1917; 2: 37–41.
Hughes RA, Swan AV, Raphaël JC, Annane D, van Koningsveld R, van Doorn PA. Immunotherapy for Guillain-Barré syndrome: a systematic review. Brain 2007; 130: 2245–57.
Ilyas AA, Willison HJ, Quarles RH, Jungalwala FB, Cornblath DR, Trapp BD, et al. Serum antibodies to gangliosides in Guillain-Barré syndrome. Ann Neurol 1988; 23: 440–7.
Ito M, Kuwabara S, Odaka M, Misawa S, Koga M, Hirata K, et al. Bickerstaff's brainstem encephalitis and Fisher syndrome form a continuous spectrum: clinical analysis of 581 cases. J Neurol 2008; 255: 674–82.
Kadlubowski M, Hughes RAC. Identification of the neuritogen responsible for experimental allergic neuritis. Nature 1979; 277: 140–1.
Krücke W. Die primar entzundliche Polyneuritis unbekannter Ursache. In: Lubasch O, Henke F, Rossle G, editors. Handbuch der speziellen pathologischen anatomie und histologie. Vol. 13. Erkrankungen der peripheren Nerven. Berlin: Springer; 1955. p. 164–82.
Lampert PW. Mechanism of demyelination in experimental allergic neuritis. Electron microscopic studies. Lab Invest 1969; 20: 127–38.
Landry O. Note sur la paralysie ascendante aigüe. Gazette Hebdomadaire de Médecine et de Chirurgie 1859; 6: 472–88.
Langmuir AD, Bregman DJ, Kurland LT, Nathanson N, Victor M. An epidemiologic and clinical evaluation of Guillain-Barré syndrome reported in association with the administration of swine influenza vaccines. Am J Epidemiol 1984; 119: 841–79.
Linington C, Izumo S, Suzuki M, Uyemura M, Meyermann R, Wekerle H. A permanent rat T cell line that mediates experimental allergic neuritis in the rat *in vivo*. J Immunol 1984; 133: 1946–50.
Linington C, Lassmann H, Ozawa K, Kosin S, Mongan L. Cell adhesion molecules of the immunoglobulin supergene family as tissue-specific autoantigens: induction of experimental allergic neuritis (EAN) by P0 protein-specific T cell lines. Eur J Immunol 1992; 22: 1813–17.
Liu JX, Willison HJ, Pedrosa-Domellof F. Immunolocalization of GQ1b and related gangliosides in human extraocular neuromuscular junctions and muscle spindles. Invest Ophthalmol Vis Sci 2009; 50: 3226–32.
Louvet C, Kabre BG, Davini DW, Martinier N, Su MA, DeVoss JJ, et al. A novel myelin P0-specific T cell receptor transgenic mouse develops a fulminant autoimmune peripheral neuropathy. J Exp Med 2009; 206: 507–14.
Makowska A, Pritchard J, Sanvito L, Gregson N, Peakman M, Hayday A, et al. Immune responses to myelin proteins in Guillain-Barré syndrome. J Neurol Neurosurg Psychiatry 2008; 79: 664–71.
Mathey EK, Park SB, Hughes RA, Pollard JD, Armati PJ, Barnett MH, et al. Chronic inflammatory demyelinating polyradiculoneuropathy: from pathology to phenotype. J Neurol Neurosurg Psychiatry 2015; 86: 973–85.
McCombe PA, Pollard JD, McLeod JG. Chronic inflammatory demyelinating polyradiculoneuropathy. A clinical and electrophysiological study of 92 cases. Brain 1987; 110 (Pt 6): 1617–30.
McGonigal R, Rowan EG, Greenshields KN, Halstead SK, Humphreys PD, Rother RP, et al. Anti-GD1a antibodies activate complement and calpain to injure distal motor nodes of Ranvier in mice. Brain 2010; 133: 1944–60.
McKhann GM, Cornblath DR, Griffin JW, Ho TW, Li CY, Jiang Z, et al. Acute motor axonal neuropathy: a frequent cause of acute flaccid paralysis in China. Ann Neurol 1993; 33: 333–42.
McKhann GM, Cornblath DR, Ho TW, Li CY, Bai AY, Wu HS. Clinical and electrophysiological aspects of acute paralytic disease of children and young adults in northern China. Lancet 1991; 338: 593–7.
McLeod JG. Electrophysiological studies in the Guillain-Barré syndrome. Ann Neurol 1981; 9 (Suppl 1): 20–7.
Meyer zu Horste G, Mausberg AK, Cordes S, El-Haddad H, Partke HJ, Leussink VI, et al. Thymic epithelium determines a spontaneous chronic neuritis in Icam1(tm1Jcgr)NOD mice. J Immunol 2014; 193: 2678–90.
Miller JAL, Spyropoulos A, Jaros E, Galban-Horcajo F, Whittaker RG, Willison HJ. Anti-GQ1b ganglioside positive Miller Fisher syndrome – evidence of paranodal pathology on nerve biopsy. J Neuromuscul Dis 2014; 1: 191–5.
Milner P, Lovelidge CA, Taylor WA, Hughes RAC. P0 myelin protein produces experimental allergic neuritis in Lewis rats. J Neurol Sci 1987; 79: 275–85.
Odaka M, Yuki N, Hirata K. Anti-GQ1b IgG antibody syndrome: clinical and immunological range. J Neurol Neurosurg Psychiatry 2001; 70: 50–5.
Prineas JW. Acute idiopathic polyneuritis. An electronmicroscope study. Lab Invest 1972; 26: 133–47.
Prineas JW. Pathology of the Guillain-Barré syndrome. Ann Neurol 1981; 9 (Suppl 1): 6–19.
Quincke HI. Die lumbal punction des Hydrocephalus. Berl Klin Wochenschrift 1891; 28: 929–33.
Salomon B, Rhee L, Bour-Jordan H, Hsin H, Montag A, Soliven B, et al. Development of spontaneous autoimmune peripheral polyneuropathy in B7-2-deficient NOD mice. J Exp Med 2001; 194: 677–84.
Sejvar JJ, Baughman AL, Wise M, Morgan OW. Population incidence of Guillain-Barré syndrome: a systematic review and meta-analysis. Neuroepidemiology 2011a; 36: 123–33.
Sejvar JJ, Kohl KS, Gidudu J, Amato A, Bakshi N, Baxter R, et al. Guillain-Barré syndrome and Fisher syndrome: case definitions and guidelines for collection, analysis, and presentation of immunization safety data. Vaccine 2011b; 29: 599–12.
Su MA, Davini D, Cheng P, Giang K, Fan U, DeVoss JJ, et al. Defective autoimmune regulator-dependent central tolerance to myelin protein zero is linked to autoimmune peripheral neuropathy. J Immunol 2012; 188: 4906–12.
Susuki K, Nishimoto Y, Yamada M, Baba M, Ueda S, Hirata K, et al. Acute motor axonal neuropathy rabbit model: immune attack on nerve root axons. Ann Neurol 2003; 54: 383–8.
Umapathi T, Tan EY, Kokubun N, Verma K, Yuki N. Non-demyelinating, reversible conduction failure in Fisher syndrome and related disorders. J Neurol Neurosurg Psychiatry 2012; 83: 941–8.
Uncini A, Kuwabara S. Electrodiagnostic criteria for Guillain-Barré syndrome: a critical revision and the need for an update. Clin Neurophysiol 2012; 123: 1487–95.
van den Berg B, Bunschoten C, van Doorn PA, Jacobs BC. Mortality in Guillain-Barré syndrome. Neurology 2013; 80: 1650–4.
van den Berg B for the IGOS consortium. The international Guillain-Barré study (IGOS): a prospective study on clinical and biological predictors of disease course and outcome. Glasgow: Inflammatory Neuropathy Consortium Meeting; 2016. Abstract book p. 55–6.
van Koningsveld R, Steyerberg EW, Hughes RA, Swan AV, van Doorn PA, Jacobs BC. A clinical prognostic scoring system for Guillain-Barré syndrome. Lancet Neurol 2007; 6: 589–94.
Waksman BH, Adams RD. Allergic neuritis: experimental disease of rabbits induced by the injection of peripheral nervous tissue and adjuvants. J Exp Med 1955; 102: 213–25.

Waksman BH, Adams RD. A comparative study of EAN in the rabbit, guinea-pig and mouse. J Neuropathol Exp Neurol 1956; 15: 293–310.

Walgaard C, Lingsma HF, Ruts L, Drenthen J, van Koningsveld R, Garssen MJ, et al. Prediction of respiratory insufficiency in Guillain-Barré syndrome. Ann Neurol 2010; 67: 781–7.

Westphal C. Ueber einige Bewegungs-Erscheinungen an gelähmter Gliedern. Arch Psychiatr Nervenkr 1875; 4: 803–34.

Wiederholt HM, Mulder DW, Lambert EH. The Landry Guillain-Barré Strohl syndrome of polyradiculoneuropathy—historical review report on 97 patients and present concepts. Proc Mayo Clin 1964; 49: 427–51.

Willison HJ. The translation of the pathological findings described in humans to experimental models of acute motor axonal neuropathy. J Peripher Nerv Syst 2012; 17 (Suppl 3): 3–8.

Willison HJ, Goodfellow JA. GBS100: celebrating a century of progress in Guillain-Barré syndrome. La Jolla: Peripheral Nerve Society; 2016. p. 1–558.

Willison HJ, Halstead SK, Beveridge E, Zitman FM, Greenshields KN, Morgan BP, et al. The role of complement and complement regulators in mediating motor nerve terminal injury in murine models of Guillain-Barré syndrome. J Neuroimmunol 2008; 201–202: 172–82.

Willison HJ, Jacobs BC, van Doorn PA. Guillain-Barré syndrome. Lancet 2016; 388: 717–27.

Yuki N, Taki T, Inagaki F, Kasama T, Takahashi M, Saito K, et al. A bacterium lipopolysaccharide that elicits Guillain-Barré syndrome has a GM1 ganglioside-like structure. J Exp Med 1993; 178: 1771–5.