Guillain-Barré syndrome

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Guillain-Barré syndrome is the most common and most severe acute paralytic neuropathy, with about 100 000 people developing the disorder every year worldwide. Under the umbrella term of Guillain-Barré syndrome are several recognisable variants with distinct clinical and pathological features. The severe, generalised manifestation of Guillain-Barré syndrome with respiratory failure affects 20–30% of cases. Treatment with intravenous immunoglobulin or plasma exchange is the optimal management approach, alongside supportive care. Understanding of the infectious triggers and immunological and pathological mechanisms has advanced substantially in the past 10 years, and is guiding clinical trials investigating new treatments. Investigators of large, worldwide, collaborative studies of the spectrum of Guillain-Barré syndrome are accruing data for clinical and biological databases to inform the development of outcome predictors and disease biomarkers. Such studies are transforming the clinical and scientific landscape of acute autoimmune neuropathies.

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Introduction

The clinical journey through Guillain-Barré syndrome follows a typical pattern that can be readily divided into its constituent phases and components (figure 1).[1] Demyelinating and axonal forms of the syndrome occur in varying proportions across different geographical regions, and clinical variants, such as Miller Fisher syndrome, are readily definable.[2] Within the typical disease course are many less well understood biological variations, which are considered chronologically in this Seminar.

First, Guillain-Barré syndrome is usually preceded by infection or other immune stimulation that induces an aberrant autoimmune response targeting peripheral nerves and their spinal roots.[3,4] Molecular mimicry between microbial and nerve antigens is clearly a major driving force behind the development of the disorder, at least in the case of *Campylobacter jejuni* infection. However, the interplay between microbial and host factors that dictates if and how the immune response is shifted towards unwanted autoreactivity is still not well understood.[5] Furthermore, genetic and environmental factors that affect an individual's susceptibility to develop the disease are unknown.[6] Unwanted autoimmunity does not arise in most individuals (>99%) exposed to an immune stimulus as a result of Guillain-Barré syndrome-associated infections such as *C jejuni*.[7]

The acute progression of limb weakness, often with sensory and cranial nerve involvement 1–2 weeks after immune stimulation, proceeds to its peak clinical deficit in 2–4 weeks.[8] When patients present with rapidly progressive paralysis, the diagnosis of Guillain-Barré syndrome needs to be made as soon as possible. Although establishment of the diagnosis in typical cases is usually straightforward, there are many clinical and investigative components to consider, especially in atypical cases. The diagnosis is largely based on clinical patterns, because diagnostic biomarkers are not available for most variants of the syndrome. Identification of biomarkers and establishment of their pathophysiological roles, if any, in experimental models has been a major research challenge.[9,10] All patients with Guillain-Barré syndrome need meticulous monitoring and supportive care.[11] Early initiation of intravenous immunoglobulins (IVIg) or plasma exchange is of proven benefit and crucial, especially in patients with rapidly progressive weakness.[12] Because a quarter of patients need artificial ventilation and many develop autonomic disturbances, many patients need admission in the high or intensive care setting. Symptoms peak within 4 weeks, followed by a recovery period that can last months or years, as the immune response decays and the peripheral nerve undergoes an endogenous repair process.

Efforts focus on the measurement and prediction of clinical course and outcome to improve the care and treatment of individual patients.[13] Good prognostic models have been developed, but additional studies are needed to investigate whether these prognostic factors differ between different disease subgroups and areas in the world. In parallel, prognostic biomarkers now need to be developed to better predict outcomes and guide action, such as personalised treatment refinements in acute management.[14] Finally, the impact of Guillain-Barré syndrome on individuals and as a global health issue is discussed alongside efforts to create evidence-based uniformity in the management of affected patients in different health-care settings.

Epidemiology and preceding infections

Most studies that estimate incidence rates of Guillain-Barré syndrome were done in Europe and North America, and showed a similar range of 0·8–1·9 (median 1·1) cases per 100 000 people per year.[15] The annual incidence rate of

Search strategy and selection criteria

We searched the entire Cochrane Library, MEDLINE, and PubMed using the search term "Guillain-Barré syndrome". We mainly selected publications from the past 5 years, but did not exclude commonly referenced and highly regarded older publications. We also searched the reference lists of articles identified by this search strategy and selected those papers we judged relevant. Review articles are cited to provide readers with more details and references than can be provided in this Seminar.