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## Review Article

## Guillain–Barré syndrome – Literature overview

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## ABSTRACT

**Introduction:** Guillain–Barré syndrome (GBS) is one of the most prevalently acquired polyneuropathies. In the past, once regarded as separate disease, now it is described as a group of few acute neuropathy subtypes of autoimmune origin. Although this disease may occur at any stage of life, equally affecting both women and men, the risk increases with age and is relatively low in children.

**Aim:** Aim of this work is to present pathogenesis, clinical picture, as well as current diagnostic methods and treatment of GBS.

**Discussion:** Although GBS is usually preceded by a mild virus infection, sometimes it is associated with a bacterial infection affecting either respiratory or digestive system. Initial symptom of classic form of GBS is usually a symmetrical paresis of proximal part of lower limbs, which gradually expands affecting upper limbs and trunk muscles. In case of diaphragmatic and intercostal nerves involvement, muscle weakness eventually leads to respiratory failure. As paralysis continues, deep reflexes tend to weaken and disappear. Diagnosis of GBS is carried out on the basis of clinical picture, cerebrospinal fluid analysis and electrophysiological study. The range and type of treatment mainly depend on severity of clinical signs and a phase of the disease.

**Conclusions:** Diagnosis and treatment of GBS are crucial issues in clinical practice, because approximately 25% of patients can develop respiratory failure, significant disability followed by GBS present in 20%, and chronic fatigue in 60%–70% of patients. Despite symptomatic treatment and immunotherapy, mortality associated with GBS still ranges from 4% to 15%.

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## 1. Introduction

Guillain–Barré syndrome (GBS), or otherwise Landry–Guillain–Barré–Strohl syndrome, was described in 1916. Haymaker and Kernohan elaborated on clinical and histopathological picture

of the disease.<sup>1</sup> GBS is one of the most commonly acquired polyneuropathies. In the past, once regarded as a separate disease, now it is rather described as a group of few acute neuropathy subtypes of autoimmune origin. Incidence of GBS in Poland is about 1.5–4 persons per 100 000 population, which accounts for about 800 new cases per year. Frequency of GBS in

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children is approx. 0.5–1.5 over 100 000 population – characterized by a milder course of the disease, however CNS symptoms like dizziness, headaches, optic disk swelling, or positive meningeal signs are more prevalent.<sup>2</sup> This disease can occur at any stage of life, equally affecting both women and men, nevertheless some reports indicate that lately it is men who suffer more often. The risk of developing GBS increases with age and while frequency of poliomyelitis has decreased, GBS became the most frequent acute disease that leads to paresis in Western countries. Despite intensive treatment, GBS mortality ranges from 4% to 15%.<sup>3,4</sup>

## 2. Aim

Aim of this paper is to present pathogenesis, clinical picture, as well as current diagnostic methods and treatment of GBS.

## 3. Discussion

GBS has been divided into few types accommodating differences in the pattern of paresis, function of affected fibers, as well as pathologic process. Classic form of GBS is an acute inflammatory demyelinating polyradiculoneuropathy – around 90% of all cases in Europe and USA. Acute motor axonal neuropathy without features of demyelination and with damage to motor nerves in Europe accounts for approx. 5% of all cases; meanwhile in China this course of the disease is characteristic for 70% of GBS.<sup>5</sup> Acute motor and sensory axonal neuropathy with motor and sensory nerve involvement is associated with more severe course of the disease. Miller-Fisher syndrome accompanied by ophthalmoplegia, ataxia and areflexia is a rather rare form of disease.

During the course of GBS, damage to nerves occurs through autoimmunologic mechanisms. Simplifying, destruction is based on demyelination in classical form of GBS and on damage of axons in initial axonal form. Ultimately it has been proved that activated lymphocytes T and antibodies, especially those against gangliosides contribute to the pathogenesis of the disease.<sup>6</sup>

In 75% of patients, GBS morbidity is usually precluded by bacterial or virus infection of either respiratory or digestive tract, few weeks prior to occurrence of first neurological signs. Until now few microorganisms have been identified and associated with GBS: *Campylobacter jejuni*, *Cytomegalovirus*, *Mycoplasma pneumoniae*, *Epstein-Barr virus*, *Haemophilus influenzae*.<sup>7</sup> It is believed that the triggering factor responsible for an infection can be identified in 25%.<sup>8</sup> Currently relation between presence of antibodies against gangliosides and preceding *C. jejuni* infection, as well as theory that those antibodies cross-react with host's gangliosides is doubtless.<sup>9</sup>

In 1976 in USA an increase in incidence of GBS has been reported after vaccination against influenza virus.<sup>10</sup> Moreover new cases were described after use of general anesthesia, after delivery, or surgical procedures, as well as other factors.<sup>11,12</sup> It has to be emphasized that GBS is not associated with genetic inheritance and in 30% of cases no specific triggering factor is established.

### 3.1. Signs and symptoms

Neurodeficiency symptoms usually appear within first 2–28 days and the course of a disease occurs in a single phase fashion in 90% of patients; the remaining group of patients develop a chronic or recurrent condition. In spite of general good prognosis in 20% of patients, development of respiratory failure is highly probable. Death occurs in 3%–5% of patients (some references state 4%–15% mortality rate) usually due to cardiovascular complications. Relapses are common and frequently may follow infections or vaccinations, even many years (4–36) after the first episode. Between relapses of the disease neurodeficiency sustained or patients were completely free of any symptoms.<sup>1,13–15</sup>

Pain occurring few days after infection and confined to interscapular and lumbar region could be very informative about the onset of the disease as it is associated with nerve roots swelling and meningeal irritation. In this period it is possible to observe in patients neck stiffness and positive Kernig's sign. Some patients complain about painful paresthesia and hypoesthesia, sometimes preceding occurrence of motor signs.<sup>16</sup> Paresis usually affects lower limbs first, often in proximal part; it gradually expands affecting upper limbs and trunk muscles. Intercostal and diaphragmatic nerves involvement leads to respiratory insufficiency. As paresis progresses, deep reflexes diminish. After the period characterized by increase of symptoms severity (till 3 weeks in 80% of patients) a plateau phase comes around (10–14 days) followed by remission phase that lasts 6–14 months in case of severe paresis. Approximately 30%–50% of patients develop cranial nerves involvement (facial, glossopharyngeus, vestibulocochlear, oculomotor, trigeminus). Disturbance of proprioception (alignment, vibration) is more frequent rather than disturbance of superficial sensation (subjective and objective). Patients experience signs of radiculopathy and myalgia. In about 30% of patients autonomic symptoms are present and should they apply to cardiovascular system, a direct threat to life is created especially for elderly patients.<sup>17–19</sup>

### 3.2. Diagnosis

Diagnosis of GBS mostly relies on clinical picture (progressive paresis of lower and upper limbs, sensation loss, cranial nerves involvement, especially facial, autonomic dysfunction), cerebrospinal fluid analysis (increase in protein concentration, increase in mononuclear leukocytes count that does not exceed 10 cells in 1 mm<sup>3</sup>), electrophysiological study (decrease of conduction velocity in motor and sensory fibers, as well as significant prolongation of distal latencies, and presence of conduction block – informative about demyelinating nerve damage).

GBS should be differentiated from other diseases and disturbances causing acute muscle weakness e.g. myasthenia, periodic paralysis, myelitis transversa, poliomyelitis, brain-stem inflammation, porphyrias and other neuropathies.

### 3.3. Treatment

Each patient, suspected of having GBS should be hospitalized because of highly variable character of the disorder, as well as

lack of possibility to predict symptoms intensity and their progress. Extent and method of treatment highly depend on patient's clinical status and phase of the disease. Patients who experience a rapid increase in symptoms' intensity require treatment in intensive therapy department with constant monitoring of basic life functions with special attention to respiratory and heart function. Plasmapheresis is considered as primary treatment and its effectiveness has been confirmed in few clinical studies.<sup>20</sup> It is an invasive method of treatment, used in specialized centers, only in cases of precise clinical recommendations, that include patients fulfilling at least one of the following criteria: respiratory failure, inability to move independently, bulbar palsy.<sup>4</sup> Usually three to five plasmapheresis sessions are carried out every second day and during one procedure about 50 mL of blood plasma per 1 kg of body weight is being exchanged. While the patient undergoes treatment it is essential to monitor blood pressure, heart's electrical activity (ECG), and follow complete blood count before and after the procedure. Plasmapheresis is not performed in patients who show ability to walk independently.<sup>20,21</sup> Treatment has to be initiated during the first two weeks since the onset of disease.

Intravenous therapy with immunoglobulins given as 0.4 g/kg dose over five following days is equally effective in treatment of severe cases of GBS.<sup>22,23</sup> Connection of both methods does not provide any additional benefit since their synergic action has not been observed. This is why in many immunology centers intravenous immunotherapy has become a treatment of choice as it carries less risk for complications. Treatment has to be implemented within first two weeks of onset of the disease, and it is not recommended in walking patients, similarly as in the case of plasmapheresis.

Autonomic disturbances and pain present in GBS have to be managed through symptomatic treatment. Patients with GBS need to be introduced to physiotherapy and psychotherapy program.<sup>24</sup> Rehabilitation should be implemented from the very first days of the disease, and program has to be individually adjusted to every patient.<sup>25</sup> Physiotherapy ought to be complex in character while appropriate kinesiotherapy, adjusted to the phase of disease and severity of symptoms plays a significant role in complications' prophylaxis, correcting muscle weakness and verticalisation.<sup>26</sup> Application of traditional exercises, i.e. passive exercise, assisted, active, non-weight bearing, and neuromuscular reeducation exercises shortens the time of reaching full recovery. Very good results are obtained with the use of proprioceptive neuromuscular facilitation method.<sup>27</sup>

Rehabilitation program should also consist of tactile stimulation of exteroceptors through touch, squeezing, grooming and proprioceptors, as well as classical massage, targeted toward correction of tissue viability in areas of decreased muscle movement: limbs, trunk, and face.

Rehabilitation of respiratory system that is needed by most of the patients, is targeted toward correction of respiratory function, enhancement of chest mobility, sustaining appropriate ventilation, increase of respiratory muscles strength, and enhancement of sputum evacuation. All of these goals can be accomplished by the use of adequate postural drainage position, chest vibromassage, nebulization, respiration exercises, and chest tapping. Rehabilitation program should be

constantly modified, and changes ought to be preceded by a thorough evaluation of patient's health status.

#### 4. Conclusions

1. Diagnosis and treatment of GBS are important issues in clinical practice, because as much as 25% of patients can develop respiratory insufficiency.
2. Significant disability following remission of GBS is present in approx. 20% of patients, and chronic fatigue is associated with 60%–70% of patients.
3. In spite of significant progress in treatment, GBS mortality accounts for 4%–15% and this is why early diagnosis, appropriate treatment and prophylaxis of complications are of great importance.

#### Conflict of interest

None declared.

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