

Variants - Chronic and Acute



**Guillain Barre Syndrome
Support Group N. Z. Trust**

Contact Us at www.gbsnz.org.nz
or The National Coordinator at
tonypearson@xtra.co.nz

03 540 3217 / 027 687 1953

Acute Variants

Axonal Guillain-Barré Syndrome

It had been known for some time that in severe cases of GBS, a 'bystander' effect of the demyelination of the nerve could be damage to the nerve core or axon. In 1986, Feasby et al [Brain 1986 Dec;109 (Pt 6):1115-26] reported autopsy studies on a patient with a clinical diagnosis of GBS and who had died that showed severe axonal degeneration in nerve roots and distal nerves without evidence of demyelination. It was suggested that this might represent a variant of GBS characterised by an acute axonal neuropathy.

In 1995, Griffin, Ho et al reported on their findings after investigating the yearly epidemic of GBS amongst children in northern China [Brain 1995 Jun;118 (Pt 3):577-95, 597-605]. Twelve autopsied cases were studied. Three of the twelve cases showed the same characteristics of classic demyelinating GBS (AIDP). Six cases showed predominantly axonal damage with only minimum demyelination. (Paradoxically, the other three cases showed only mild changes to the nerve roots and sciatic nerves.) Within the group of six that showed axonal damage, three showed damage to both motor and sensory nerves and three had damage almost exclusively to the motor nerves. The patterns were described as acute motor-sensory axonal neuropathy (AMSAN) and acute motor axonal neuropathy (AMAN).

Of 129 Chinese patients who were studied, 65% had the axonal form, 24% the demyelinating form and 11% could not be classified. One batch of 38 patients (55% axonal, 32% demyelinating, 13% unclassified) was tested for antibodies to the bacterium *Campylobacter jejuni*. Sixty-six percent of the 38 showed evidence of recent *Campylobacter jejuni* infection compared with 16% in the control).

It did not take long for the axonal neuropathy as described by Feasby et al and the 'Chinese paralytic syndrome' to be regarded as one and the same and it was quickly recognised that *Campylobacter jejuni* was probably the most common trigger for GBS in the West as it seemed to be in China. [Hughes RA, Rees JH, Infect Dis 1997 Dec;176 Suppl 2:S92-8]

In 1997, Ho et al reported [Neurology 1997 Mar;48(3):717-24] on the mechanisms of paralysis and recovery during AMAN. The most severe cases showed degradation of motor axons affecting the ventral roots as well as the peripheral nerves. In contrast, a patient with the characteristic findings of AMAN recovered quickly after plasmapheresis. A sural nerve biopsy proved normal but a biopsy at a neuromuscular junction showed denervation (possibly explaining the Chinese paradox). Antibodies have also been found to be binding to the nodes of Ranvier (between the myelin segments) preventing transmission. There are clearly different mechanisms at work here: one resulting in a slow and incomplete recovery and another resulting in a rapid recovery.

Note:

Chinese AMAN patients had been found to recover at an identical rate as Chinese AIDP patients suggesting they fell into the latter category.

So while some patients with 'axonal GBS' may recover quickly, others have considerable axonal damage. They will be joined by those who have bystander axonal damage as a result of AIDP (and indeed CIDP). The only proven treatments are plasma exchange and IVIg (AIDP) plus corticosteroids (CIDP). A problem arises because while demyelination appears to be effectively and promptly repaired by remyelination, axonal degeneration can cause severe persistent disability.

[Hughes et al, *Mult Scler* 1997 Apr;3(2):88-92].

For the possible consequences of Severe GBS, see our guide *After GBS – Severe GBS Supplement*.

Miller Fisher Syndrome

Miller Fisher syndrome (MFS) is also known as:

- The Miller Fisher variant [of GBS]
- Fisher or Fisher's syndrome
- acute idiopathic ophthalmologic neuropathy
- syndrome of ophthalmoplegia, ataxia and are flexia

Related conditions are:

- GBS with ophthalmoplegia
- Bickerstaff's brainstem encephalopathy
- acute ophthalmoparesis

In 1956, Charles Miller Fisher, a Canadian whose specialisation was stroke, described three patients with acute external ophthalmoplegia (eye paralysis), sluggish pupil reflexes, ataxia (lack of balance) and areflexia (absent tendon reflexes). Two patients had no weakness; the other had a facial palsy and possible weakness. All three recovered spontaneously.

Because some patients with GBS had ophthalmoplegia and there were other similarities, Dr Fisher concluded that these patients had suffered a disorder akin to GBS. [Fisher CM. Syndrome of ophthalmoplegia, ataxia and areflexia. *N Engl J Med* 1956;255:57-65] Pure Miller Fisher syndrome (without generalised weakness) is rare. Electrodiagnostic abnormalities found in all patients are characteristic of an axonal neuropathy or a neuronopathy with predominant sensory nerve changes in the limbs and motor damage in the cranial nerves. [Fross RD, Daube JR. Neuropathy in the Miller Fisher syndrome: clinical and electrophysiologic findings. *Neurology* 1987 Sep;37(9):1493-1498] Patients described as having Miller Fisher syndrome often have a neuropathy that overlaps with GBS and demonstrate generalised weakness, sometimes paralysis, as additional symptoms. It was sometimes proposed the Miller Fisher syndrome was caused by brainstem encephalitis. It is true that the syndrome can be mimicked by a brainstem lesion, but typical cases of Miller Fisher syndrome rarely show any evidence of brainstem abnormalities either radiologically or during post-

mortem examination. When clinical or radiological brainstem abnormalities are found, the condition may be referred to as Bickerstaff's syndrome or Bickerstaff's brainstem encephalopathy (or encephalitis) (BBE).

Research in recent years has concentrated in identifying the antibodies that are thought to be responsible for GBS etc. It has been confirmed clinically that MFS, GBS with ophthalmoplegia, BBE, and another condition called acute ophthalmoparesis* are closely related, forming a continuous range. This is supported by immunological findings with the antibody anti-GQ1b IgG being the common factor. [J Neurol Neurosurg Psychiatry 2001 Jan;70(1):50-55] This antibody is not found in other GBS patients so it is thought that it is responsible for the ophthalmoplegia. *Acute ophthalmoparesis (AO) is characterised by acute onset of paresis of the extraocular muscles without ataxia or areflexia.

It has been further noted that many BBE patients have limb weakness and this is considered as an overlap with axonal GBS indicating the disorders are related. [Yuki, Rinsho Shinkeigaku 2004 Nov;44(11):802-4.

Although the efficacy has not been clinically proven, treatment of Miller Fisher syndrome is much the same as 'classic' GBS though the different symptoms require modified management with emphasis on the eyes. Intravenous immunoglobulin or plasma exchange treatment is likely in all but the mildest cases. The chances of recovery are good.

Chronic Variants

Paraproteinaemic demyelinating neuropathy

Paraproteinaemic demyelinating neuropathy (PDN) is sometimes described as:

- chronic demyelinating neuropathy associated with a benign paraprotein;
- CIDP associated with paraprotein;
- CIDP with paraproteinaemia.

Antibody-producing bone marrow cells go out of control and produce large numbers of the same antibody. The antibody (or immunoglobulin) sometimes damages nerve fibres causing a peripheral neuropathy.

Some doctors regard the clinical, electrophysiological and pathological features of the demyelinating paraproteinaemic neuropathies and of CIDP as closely similar and almost indistinguishable.

These neuropathies are usually late-onset in terms of age and are mixed motor and sensory, although the severity of sensory loss tends to be greater compared with CIDP. So there is usually more pain but less severe weakness and impairment.

Most patients respond to corticosteroids, cytotoxic drugs, or plasma exchange. Group member Ken Sawyer has created a Web site of information on PDN. The GBS Support Group accepts no responsibility for linked sites.

Multifocal motor neuropathy

Multifocal motor neuropathy (MMN) mimics motor neurone disease (MND/ALS). Research has shown it to be a chronic demyelinating neuropathy and some regard it as a rare variant of CIDP. However, there are differences that are more prominent than the similarities. MMN patients commonly have asymmetric weakness of the distal (far) muscles, while in CIDP, proximal (near) symmetric weakness is more common. The remitting and relapsing course that may occur in CIDP is uncommon in MMN. Patients with MMN rarely have significant sensory symptoms, unlike CIDP. Increased protein level in the cerebrospinal fluid of MMN patients is rare.

Treatment by IVIg or cyclophosphamide is shown to be effective.

Lewis-Sumner syndrome or MADSAM

The Lewis-Sumner syndrome is also known as MADSAM — multifocal acquired demyelinating sensory and motor neuropathy. It is a chronic condition with similarities to multifocal motor neuropathy but with enough differences, especially in treatment, to have acquired its own definition. Some report it to be an asymmetrical variant of CIDP.

MMN and MADSAM respond to IVIG. Some MADSAM sufferers respond to prednisolone whilst most MMN sufferers do not.

Chronic axonal neuropathy

Chronic axonal neuropathies are common, particularly as a result of diabetes or alcoholism. However, the medical literature does report cases of immune-mediated chronic axonal neuropathy though there are suggestions that this is a secondary result of myelin damage that ultimately appears to be the primary cause of the condition.

Sub-acute inflammatory demyelinating polyradiculoneuropathy (SIDP)

GBS is defined when the nadir (worst point) occurs within four weeks of first symptoms. Usually it is much less. CIDP is defined when the nadir comes after eight weeks. Usually it takes much longer. An illness peaking after four weeks but before eight weeks may be called subacute etc and will be treated as CIDP or GBS depending on which it best resembles.

For the possible consequences of Severe GBS, see our guide *Recovery Advice - Severe Residual Effects of GBS*.

This series of guides is produced by the Guillain-Barré syndrome Support Group. Our guides are easily downloaded from our website in PDF format and may be both read and printed using free Adobe Reader software. Alternatively you can request printed copies from the office.

The GBS Support Group is a registered charity and receives neither government nor Lottery funding. If you have found this guide helpful and would like to help us to continue publishing copies for others affected by GBS and its related conditions, please consider making a donation to the Support Group. Secure donations may be made on line. Alternatively you can request a form from our office.

