

Guillain-Barre Syndrome

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ABSTRACT

Guillain-Barre syndrome is an acute, or more often, a subacutely evolving paralytic disease of unestablished etiology. The condition is often designated as the Landy-Guillain-Barre-Strohl syndrome in recognition of the descriptions provided by Landy in 1859 and again in 1916 by Guillain, Barre and Strohl. The pathogenesis and specific therapy in this condition remains imperfectly defined. The diagnosis is usually clinical with supportive laboratory tests. In this syllabus, we review the diagnostic criteria in Guillain-Barre syndrome and current therapies in the acute management followed by presentation of the acute management protocol used in the Neurosciences Department at the Riyadh Armed Forces Hospital.

Keywords: Peripheral neuropathy, Guillain-Barre syndrome, nerve conduction studies, plasmaphoresis, intravenous immunoglobins.

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Guillain-Barre syndrome (GBS) is now recognized to be a diverse disorder that can be divided into several patterns based on the predominant mode of fibre injury (demyelinating versus axonal) and on nerve fibres involved (motor, sensory and motor, or cranial). The most frequent pattern is the acute inflammatory demyelinating polyradiculoneuropathy (AIDP). Acute inflammatory demyelinating polyradiculoneuropathy is an acute inflammatory demyelinating polyradiculoneuropathy characterised by lymphocyte and macrophage infiltration and destruction of the myelin. The incidence of GBS ranges from 0.6-2.4 cases per 100,000 population per year.¹ It occurs in all parts of the world and at all age. Also, it occurs sporadically but outbreaks have been reported. Guillain-Barre syndrome often occurs after a viral infection such as cytomegalovirus, Epstein Barre virus, small pox vaccinia, HIV and other viruses.¹ The association to bacterial infection is also seen such as mycoplasma, brucella, and campylobacter jejuni (CJ). Acute inflammatory demyelinating polyradiculoneuropathy, acute motor axonal neuropathy (AMAN), and acute motor

sensory axonal neuropathy (AMSAN) are seen with CJ.²

Clinical Manifestations. The major clinical manifestations include weakness, which evolves symmetrically over several days and is complete after 2 weeks in 50% of cases and after 4 weeks in over 90% of cases. In most instances, the weakness is noticed initially in the legs but can begin in the arms or the face. Proximal and distal muscles of the limbs are involved. Facial diplegia is seen in at least 50% of cases. Symmetrical involvement of extraocular muscles has been described. Oropharyngeal dysfunction is observed in severe cases and can be viewed as a herald of impending respiratory failure, which usually occurs in the presence of limb and trunk weakness. The external urethral sphincter is involved in 10-20% of cases. Mild distal paresthesia often occur early in the course of the disease. On presentation, deep tendon reflexes are diminished or absent in 75% and, later in the course, almost 95% of the patients have areflexia. Autonomic function is often abnormal manifesting as sympathetic or parasympathetic over activity or deficiency or as a mixture of both. Sinus tachycardia occurs in more

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than 50% of severe cases other autonomic symptoms, which include bradycardia, facial flushing, orthostatic hypotension or fluctuating hypertension, loss of sweating or episodic diaphoresis.¹

Variants of Guillain-Barre syndrome. The most common form of GBS is AIDP, the typical presentation of which consists mild distal paresthesia and ascending paralysis within a few days, and many variations have been described. The most common variant is the Miller-Fisher syndrome, which is characterised by symmetrical ophthalmoplegia, ataxia and areflexia. Other variants include weakness without sensory involvement, paraparetic variant, pharyngeal-cervical-brachial variant, facial diplegia with distal paresthesia, acute pandysautonomia and axonal forms of GBP, i.e. acute motor axonal neuropathy (AMAN) and the acute motor sensory axonal neuropathy (AMSAN).²

Pathogenesis and pathology of Guillain-Barre syndrome. The pathogenesis of GBS has not been established.¹ Most of the evidence suggest that the disorder is a cell mediated autoimmune disease of the peripheral nerves. The prominent pathologic features in AIDP are segmental demyelination and mononuclear cellular infiltration. Infiltrates are scattered seemingly random along peripheral nerves, cranial nerves, motor and sensory roots, dorsal root ganglia and sympathetic ganglia. Ultra structurally, two patterns of myelin breakdown can be detected, contact mediated myelinolysis mediated by macrophages and vesicular disruption of myelin without inflammation perhaps mediated by cytokines.¹ Older lesions are characterised by extensive Schwann cell proliferation as a prelude to remyelination. Electrophysiological conduction of impulses through areas of segmental demyelination is severely compromised.¹ The AMAN is usually associated with Wallerian degeneration of motor fibres in the spinal roots and peripheral nerves without lymphocytic infiltration or demyelination.

Differential diagnosis of Guillain-Barre syndrome. It is necessary in acute motor paralysis to distinguish acute inflammatory demyelinating polyradiculopathy from acute myelopathy. Areflexia can be seen in both disorders at onset, however, the presence of sphincteric disturbance or the presence of a sensory level favours acute myelopathy. A history of fatigability or fluctuating ocular symptoms favours the diagnosis of myasthenia gravis. A history of recent ingestion of canned food, dilated pupils, bradycardia and constipation favour the diagnosis of acute botulism. Other differential diagnoses to be excluded lyme disease, particularly if the patient has bilateral facial palsy, brucellosis if bilateral deafness, fever, excessive sweating, joint pain and history of ingestion of raw milk, polymyositis, critical care polyneuropathy, porphyric neuropathy, heavy metal intoxication are other less likely differential

diagnoses.¹

Diagnosis of Guillain-Barre syndrome. The diagnosis of AIDP is often clinical and supported by laboratory data such as acellular cerebrospinal fluid (CSF) with high protein about a week after onset symptoms.^{1,3} Cerebrospinal fluid pleocytosis may signify an underlying infection or neoplasia.¹ Anti GM1, ganglioside antibodies are more likely frequently detected in patients with CJ infection, but also can be seen with other infections such as CMV.⁴⁻⁷ Antibodies to GQ 1b ganglioside antibodies are seen with other variants of AIDP. Anti-GT_{1a} and anti-GM_{1b} occur more frequently with the oropharyngeal variant, anti-GD_{1a} with the AMAN, and anti-GD_{1b} with sensory ataxia. To diagnose Guillain-Barre syndrome, the necessary clinical criteria include progressive symmetrical limb, weakness, hyporeflexia or areflexia, progressive of less than 4 weeks and the absence of other causes of acute neuropathy, such as porphyria or lead poisoning, etc. Supportive criteria include mild sensory signs, cranial nerve involvement particularly the facial nerve, autonomic dysfunction, cerebrospinal fluid picture of cytoalbumin dissociation with elevated protein and low cell count (WBC < 20/min) after the first week of illness and electrophysiological features.³

Electrophysiologic abnormalities in AIDP include multifocal conduction block, slowing of nerve conduction velocities, prolonged distal motor latencies and delayed F waves. Conduction studies are frequently normal in early stages of AIDP. Ancillary electrophysiological studies include blink reflexes, assessment of autonomic function with sympathetic skin response and heart rate variability.^{3,8} The proposed electrodiagnostic criteria for GBS includes three of the following four feature: 1. reduction in conduction velocity in two or more motor nerves: a. < 80% of lower limit of normal if amplitude is > 80% of the left lower limit of normal (LLN). b. < 70% of LLN if amplitude is < 80% of LLN. 2. Conduction block or abnormal temporal dispersion in one or more motor nerves either peroneal nerve between ankle and below fibular head median nerve between wrist and elbow or ulnar nerve between write and below elbow. Criteria for partial conduction block: a. < 15% change in duration between proximal and distal sites. Criteria for abnormal temporal dispersion and possible conduction block: a. > 15% change in duration between proximal and distal sites and > 20% drop in negative peak area or peak to peak amplitude between proximal and distal sites. 3. Prolonged distal latencies in two or more nerves: a. 125% of upper limit of normal (ULN) if amplitude is > 80% of LLN. b. > 150% of ULN if amplitude is < 80% of LLN. 4. Absent F-waves or prolonged minimum F-wave latencies in two or more motor nerves. a.

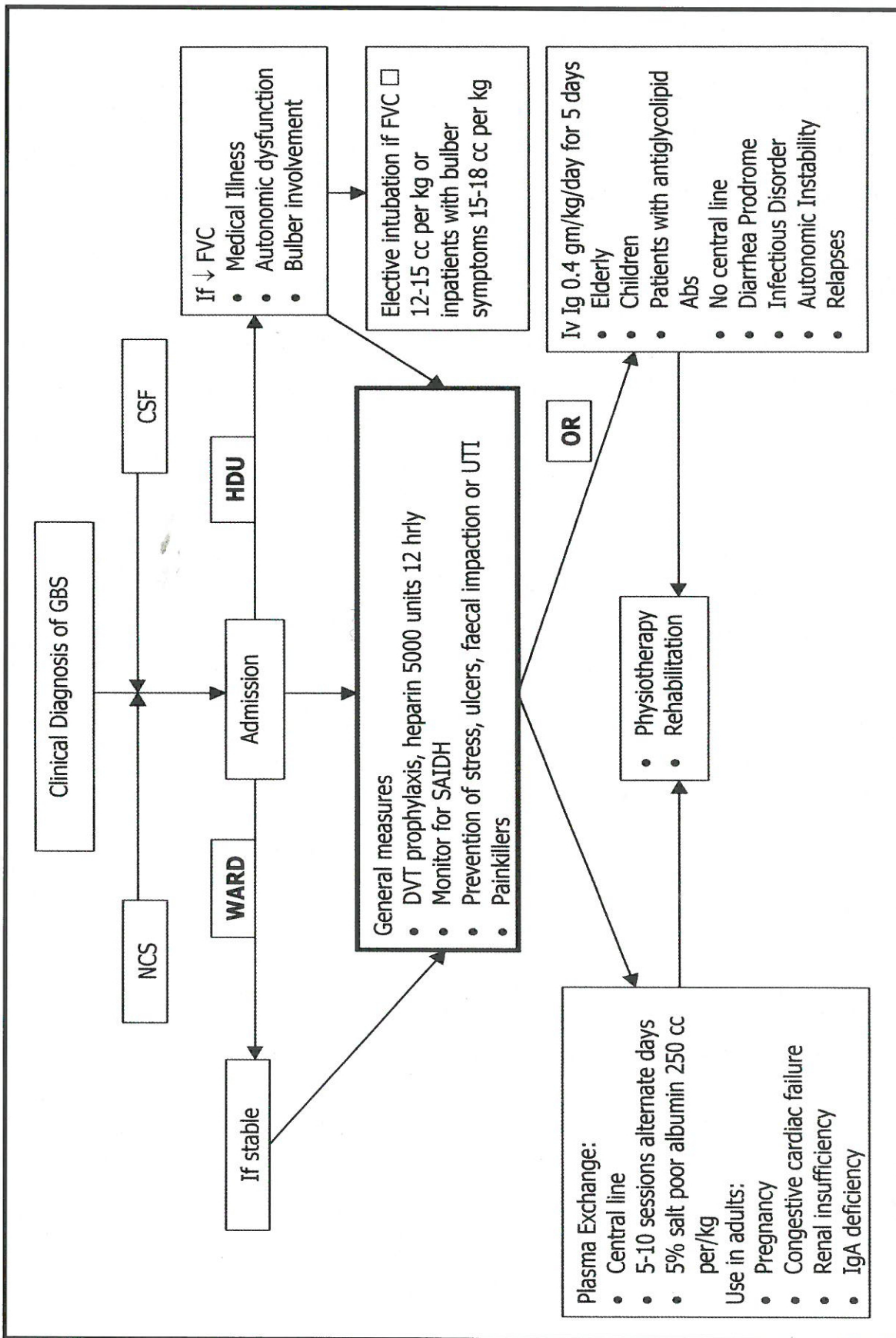


Figure 1 - Riyadh Armed Forces Hospital scheme of Guillain-Barre Syndrome management.

120% of ULN if amplitude is > 80% of LLN. b. > 150% of ULN if amplitude is < 80% of LLN.⁷ Electrodiagnostic criteria for AMAN includes early electromyographic changes of abnormal spontaneous activity, i.e. fibrillation and positive sharp waves and a decrease in motor unit recruitment on voluntary effect. Nerve conduction studies show depressed distal compound muscle action potential (CMAP) amplitude with minimal impaired motor and sensory conduction velocities, distal latencies or F-wave latencies.⁸

Management of Guillain-Barre syndrome. Treatment of GBS include supportive therapy and early plasmapheresis or intravenous immunoglobulin.⁸ Corticosteroids is not useful in the treatment of AIDP.⁹ Plasmapheresis (total of 200-250 cc/kg in 5 sessions over 7-14 days) is preferred when the adult patient comes early, especially if he has additional congestive cardiac failure, renal insufficiency, IgA deficiency or in a pregnant lady with AIDP.^{9,10} A course of intravenous immunoglobulins (IvIgG) (0.4 gm/kg/day for 5 days) is preferred in patients with GBS, if elderly or children, with no central line, autonomic stability, AMAN or AMSAN, infectious disorders or with patient who has diarrhoea prodrome or has positive anti-ganglioside antibodies.^{11,12} In relapses or severe disease, a second course of IvIgG may enhance recovery. Recent controlled clinical trials have shown that IvIgG is of equivalent efficacy to plasma exchange in the treatment of acute Guillain-Barre syndrome. No proof of increased relapse rate with IvIgG therapy. No advantage from combined therapy. Fluctuation of symptoms is unrelated to treatment modality. The efficacy of combined IvIgG and steroids is still under investigation.^{1,2}

Recovering from AIDP ranges from complete and rapid to slow with significant disability.⁸ Poor prognostic features include older age, rapid onset, assisted ventilation with active and severe axonal degeneration with denervation on electromyographic

studies.¹⁻⁸ Relapse rate is about 3% and mortality rate is 3-8%.^{1,8}

In Figure 1, we present the management protocol of GBS being followed in the Neurosciences Department at the Riyadh Armed Forces Hospital, which is used in many cases.

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