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Guillain–Barré Syndrome

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In about 20–30 % of patients with Guillain–Barré (GBS) syndrome, the disorder becomes a neurocritical illness, which not only wholly changes the clinical picture but also increases in-hospital morbidity. Neurointensivists have been taking care of these patients since the specialty came into focus and particularly after the publications on GBS from the Massachusetts General Hospital [1–3].

This year marks the 100th anniversary of the description of the disorder that would become known as Guillain–Barré syndrome (Fig. 1). On October 13, 1916, *Bulletins et Mémoires de la Société Médicale des Hôpitaux de Paris* published a paper, *Sur un syndrome de radiculo-néurite avec hyperalbuminose du liquide céphalo-rachidien sans réaction cellulaire* [4].

At the time, France was at war, and the brutal battle of the Somme was in progress. The patients, a hussar (cavalry) and an infantry soldier, were each admitted with tingling and progressive limb weakness causing major difficulty with walking. Severe weakness of all four limbs was noted with areflexia, confirmed by electrophysiologic studies performed by Andre Strohl, who found absent reflexes but retained idiomuscular contractions. One patient regained strength after 2 months. The other patient improved in the 1 month before transfer to another institution, where he was lost to further follow-up. The authors were Professors George Guillain, Jean Barré, and (little known) André Strohl. Both astute French neurologists were clinicians and prolific writers working in the neurologic center of the 6th Army in Amiens (capital of Somme Department). Their paper—published less than a month after the second patient was seen in the hospital—was also one of many published by Guillain and Barré and others that year. It must be of interest to neurointensivists to learn that several, such as *Hémiplégies par blessures de guerre* and *Les plaies de la moelle épinière par blessures de guerre* [5, 6], involved head and spine injury as a result of the Great War. In their 1916 paper, they considered (but discounted) food poisoning, trench fever with its extreme myalgias, and particularly neurosyphilis because these patients on rare occasion may had albuminocytologic dissociation. In a 1936 follow-up publication with ten additional cases, Guillain compared the excellent outcome with the much worse poliomyelitis.

Guillain and Barré themselves began referring to it as *notre syndrome* (our syndrome) several years later. Historically, but not neurologically they were successful in separating their cases from Landry's case [7]. In 1859, Landry reported a 43-year-old man with walking difficulty followed by worsening weakness involving the diaphragm, facial, laryngeal, and jaw muscles. The patient died within 1 week. Before the paralysis started, the patient complained about fevers and bouts of severe pain [8].

Guillain felt that Landry's case of acute ascending paralysis was a different condition and said the inclusion of his name totally confused the nomenclature, *Une confusion nosographique absolue* [9]. Guillain suggested poliomyelitis or acute encephalomyelitis may have been part of Landry's cases, but without much corroborating evidence of his criticism. Apart from the unexplained fever

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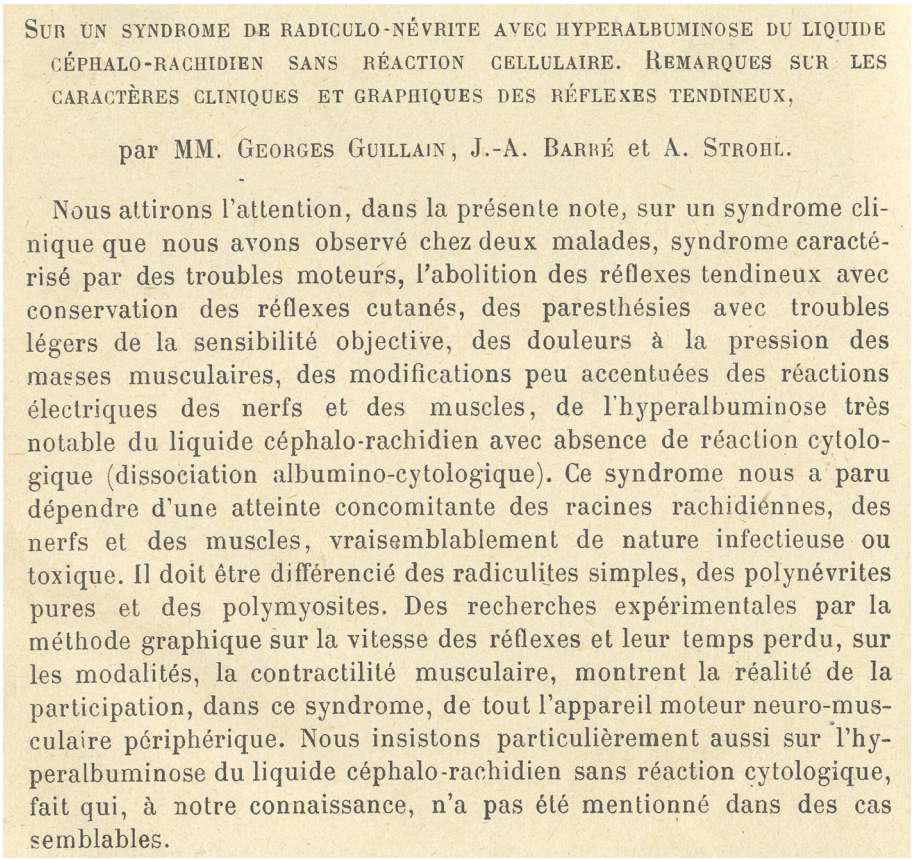

SUR UN SYNDROME DE RADICULO-NÉVRITE AVEC HYPERALBUMINOSE DU LIQUIDE CÉPHALO-RACHIDIEN SANS RÉACTION CELLULAIRE. REMARQUES SUR LES CARACTÈRES CLINIQUES ET GRAPHIQUES DES RÉFLEXES TENDINEUX,

par MM. GEORGES GUILLAIN, J.-A. BARRÉ et A. STROHL.

Nous attirons l'attention, dans la présente note, sur un syndrome clinique que nous avons observé chez deux malades, syndrome caractérisé par des troubles moteurs, l'abolition des réflexes tendineux avec conservation des réflexes cutanés, des paresthésies avec troubles légers de la sensibilité objective, des douleurs à la pression des masses musculaires, des modifications peu accentuées des réactions électriques des nerfs et des muscles, de l'hyperalbuminose très notable du liquide céphalo-rachidien avec absence de réaction cytologique (dissociation albumino-cytologique). Ce syndrome nous a paru dépendre d'une atteinte concomitante des racines rachidiennes, des nerfs et des muscles, vraisemblablement de nature infectieuse ou toxique. Il doit être différencié des radiculites simples, des polynévrites pures et des polymyosites. Des recherches expérimentales par la méthode graphique sur la vitesse des réflexes et leur temps perdu, sur les modalités, la contractilité musculaire, montrent la réalité de la participation, dans ce syndrome, de tout l'appareil moteur neuro-musculaire périphérique. Nous insistons particulièrement aussi sur l'hyperalbuminose du liquide céphalo-rachidien sans réaction cytologique, fait qui, à notre connaissance, n'a pas été mentionné dans des cas semblables.

Fig. 1 Original cover page of the seminal article

in Landry's cases, prima facie evidence suggests the case descriptions are quite similar to severely affected patients with GBS. Strohl never entered the eponym and chose another (equally prolific) career as a professor of Physical Medicine.

Gradually more severe cases of Guillain–Barré syndrome (GBS) were reported; but until the 1950s, these patients would die from respiratory arrest. A case record from Massachusetts General Hospital in 1951 described a 13-year-old girl with Guillain–Barré syndrome with 'tired' breathing and 'pharyngeal' mucus, both requiring suction and bronchoscopy and complicated by a fatal aspiration pneumonia on the 6th hospital day. In this report, a "respirator" was used, most probably a tank ventilator [10].

Bendz's important article on respiratory care in GBS begins with three patients placed in a cuirass, who *"died with gurgling mucus in the pharynx"* [11]. A fourth case, that of a 28-year-old woman rapidly progressing, again with a combination of dysphagia and respiratory distress leading to cyanosis and absent diaphragmatic breathing, was salvaged due to a promptly placed tracheostomy and connecting the patient to an Engström respirator. She was successfully weaned. This patient might have been one of the first published cases of successful respiratory care and positive-pressure mechanical ventilation in severe GBS (Fig. 2). The patient also showed EKG abnormalities (intraventricular block, widening of QRS complex, and flattening of the ST wave) and clinical signs (*…, a pulse rate about 130, and blood pressure of 245*) of "myocarditis" [11].

In the original article, Guillain, Barré, and Strohl specifically denied sphincter dysfunction [4]. The recognition of severe dysautonomia started in 1971 with Lichtenfeld's paper (Fig. 3). The neurologist, Peter Lichtenfeld from Mount Sinai Hospital New York, attributed fatality in GBS to dysautonomia. In his manuscript, 4 of 28 patients died "*during or immediately after episodes of severe autonomic dysfunction*" as a result of *"cardiac arrest following several hours of rapidly fluctuating autonomic status*" or "*found dead after extremely high blood pressure recordings although paralysis was not severe"* but also *"died suddenly after the development of a cardiac arrhythmia preceded by electrographic abnormalities.*" He emphasized that these patients with inadequate sympathetic responsiveness must be positioned carefully; straining at bowel movements must be avoided, respiratory pressures deliberately set, and a cardiac monitor employed at the first sign of autonomic

Fig. 2 Benz article on respiratory care and one of the first patients with GBS managed with positive-pressure ventilation and tracheostomy Reproduced with permission from Archives of Neurology and Psychiatry. 1955. 73(1): 22–27. Copyright© (1955) American Medical Association. All rights reserved

RESPIRATORY PROBLEMS IN ACUTE GUILLAIN-BARRÉ SYNDROME

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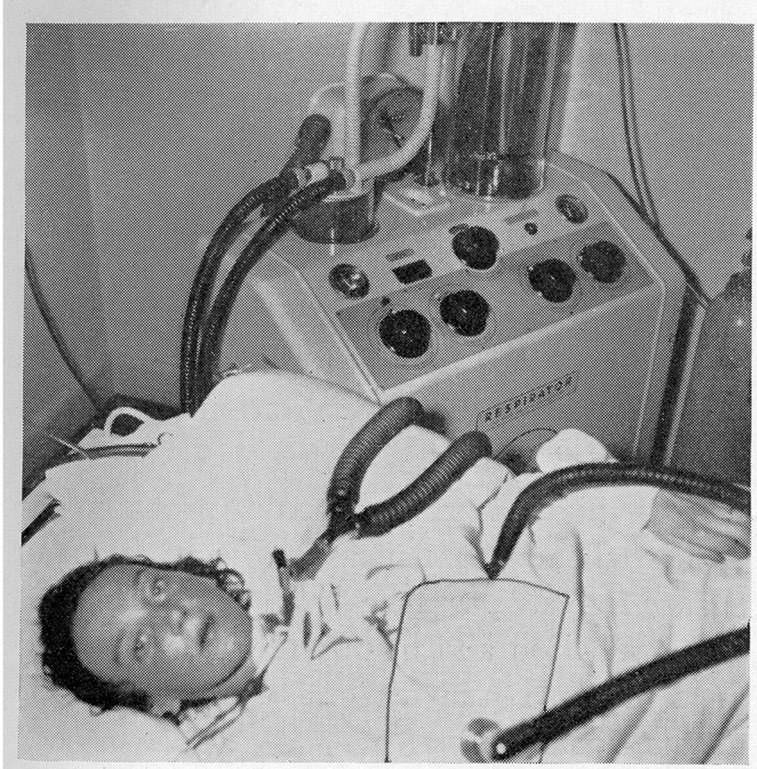
SINCE 1916, when Guillain, Barré, and Strohl [1] described two cases of radiculoneuritis with special findings in the cerebrospinal fluid (albuminocytologic dissociation), acute radiculitis has received attention throughout the world, innumerable cases having been described in the literature. Guillain's two cases were purely spinal with tetraplegia, and the prognosis quoad vitam did not come into question. But in acute polyradiculoneu ritis nerves of vital importance may be attacked, i. e., the vagus, phrenic, and intercostal nerves. In such malignant cases the prognosis quoad vitam is serious, and in the literature the mortality rate varies between 15% and 75% in undifferentiated series.*

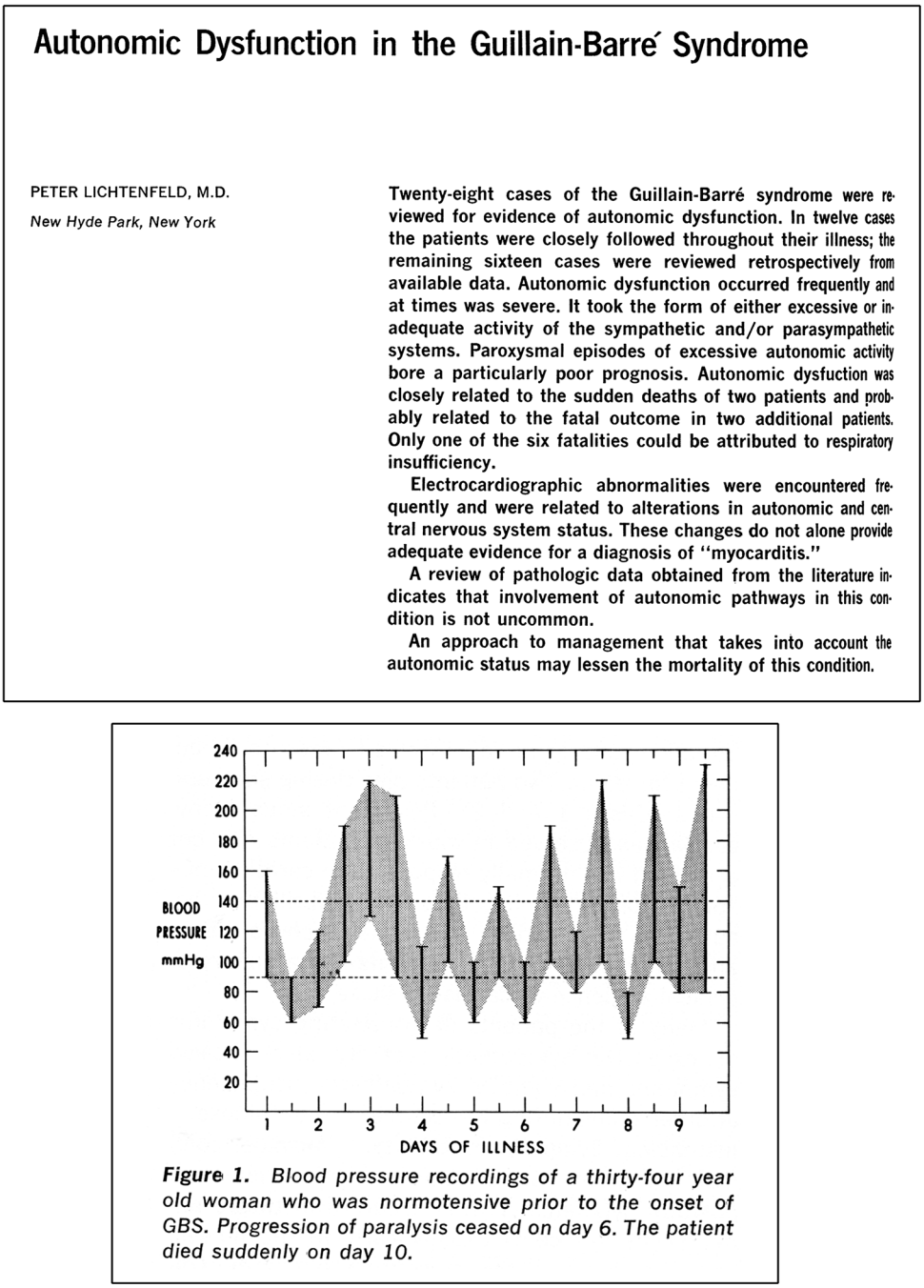
During the period from 1947 to March, 1953, the Stockholm Hospital for Infectious Diseases had a total of 15 cases of acute malignant Guillain-Barré syndrome attended by pharyngeal and respiratory paralysis, the patients comprising 11 adults and 4 children aged from 3 to 13 years. Seven (47%) of these patients required respirator treatment, nant cases is fairly consistent. The disease runs a relatively rapid course, usually about a week, and progresses toward a crisis, at which point it may be abruptly halted and then regress. The Landry type of paralysis is common. When the process commences to attack the pharyngeal and respiratory motor nerves, a life-endangering condition results. In pharyngeal paralysis quantities of mucus and saliva are formed which cannot be swallowed in the normal way but stagnate in the pharynx and run into the trachea and bronchi, with a major risk of obturation of the air passages. If the respiratory motor nerves commence to fail, there will be a threat of ventilatory insufficiency and respiratory standstill.

The condition in these malignant cases with pharyngeal and respiratory paralysis is similar to that in poliomyelitis, and the treatment, too, is largely the same. If patients with these malignant types of polyradiculitis are to survive the crisis, it is essential both to keep the air passages free by preventing aspiration of mucus and saliva and to give adequate artificial respiration, which implies sufficient oxygenation as well as elimination of carbon dioxide.

Figure 1.



dysfunction [12]. These blood pressure elevations required treatment, but he recognized that treatment could lead to a marked hypotension due to exaggerated drug sensitivity. Others reported a whole gamut of cardiac arrhythmias that were in GBS including complete heart blockage [13, 14]. (Sinus tachycardia and so-called vagal bradycardia spells remain the most frequent manifestations in patients with GBS.)



Autonomic Dysfunction in the Guillain-Barré Syndrome

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Twenty-eight cases of the Guillain-Barré syndrome were reviewed for evidence of autonomic dysfunction. In twelve cases the patients were closely followed throughout their illness; the remaining sixteen cases were reviewed retrospectively from available data. Autonomic dysfunction occurred frequently and at times was severe. It took the form of either excessive or inadequate activity of the sympathetic and/or parasympathetic systems. Paroxysmal episodes of excessive autonomic activity bore a particularly poor prognosis. Autonomic dysfuction was closely related to the sudden deaths of two patients and probably related to the fatal outcome in two additional patients. Only one of the six fatalities could be attributed to respiratory insufficiency.

Electrocardiographic abnormalities were encountered frequently and were related to alterations in autonomic and central nervous system status. These changes do not alone provide adequate evidence for a diagnosis of "myocarditis."

A review of pathologic data obtained from the literature indicates that involvement of autonomic pathways in this condition is not uncommon.

An approach to management that takes into account the autonomic status may lessen the mortality of this condition.

Figure 1. *Blood pressure recordings of a thirty-four year old woman who was normotensive prior to the onset of GBS. Progression of paralysis ceased on day 6. The patient died suddenly on day 10.*

Fig. 3 Lichtenfeld article on dysautonomia with example of blood pressure swings Reprinted from The American Journal of Medicine, Vol. 50, Lichtenfeld P., Autonomic dysfunction in the Guillain–Barré syndrome, Pages 772–780, Copyright (1971), with permission from Elsevier

Equally important was the discovery of specific treatment next to supportive treatment. Brettle et al., from Hammersmith Hospital, published one of the first studies that suggested the efficacy of plasma exchange (PLEX). They described a single case of a patient with GBS who, after a second PLEX, noted dramatic and sustained improvement of proximal limb power [15]. After four exchanges, the patient was able to sit and stand unaided. Addison et al. [16] also observed improvement in four patients with GBS by PLEX. IVIG would soon become the preferred treatment because it offered identical efficacy but with a simplified protocol of administration.

Management of GBS remains a core clinical requirement in the practice of neurocritical care. Once a severe case of GBS is admitted to the neurosciences intensive care unit management involves long-term respiratory care and

management of major blood pressure variations and cardiac arrhythmias with occasional transient use of a pacemaker. Moreover, drugs to treat dysautonomia may worsen dysautonomia (glycopyrrolate for increased secretions, neostigmine for ileus, and β blockers for tachycardia). Some organs are involved because an infection anteceded GBS but systems may potentially be injured as part of the immune target. As with so many other disorders, the full clinical picture became clear only after decades of close observation. Neurologists took exception with the benign nature of the disorder, and GBS was far more serious in some cases than originally claimed. However, patients recover even after a protracted plateau and slow rehabilitation. We should be the first to tell the patient that weaning of the ventilator and full recovery is anticipated. Our task is to get them through the first tough weeks.

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