The Legacy of the Seminal Publication by Guillain, Barré, and Strohl: The History Behind the Eponym

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ABSTRACT

The report, "On a syndrome of radiculoneuritis with hyperalbuminosis of the cerebrospinal fluid without a cellular reaction. Remarks on the clinical characteristics and tracings of the tendon reflexes," published in 1916, included superb longitudinal clinical observations of progressive areflexic paralysis in 2 French soldiers, unique laboratory findings from the still new at that time technique of lumbar puncture, and electrophysiological studies. The classic observation of the albumino-cytologic dissociation in the spinal fluid, even over 100 years later, is still one of the most important laboratory findings used by clinicians to confirm the suspected diagnosis of the Acute Inflammatory Demyelinating Polyneuropathy, typically eponymously referred to as Guillain Barré Syndrome (GBS). The contribution of André Strohl, who reported the electrophysiological abnormalities observed in their patients with novel myographic studies of tendon reflexes, led to eventual widespread use of electrodiagnostic techniques in bedside diagnosis of neuromuscular conditions. Since 1916, the clinicopathological spectrum of GBS has expanded continuously, with better understanding of the etiology, pathology, and electrodiagnostic findings. However, most of the seminal observations and conclusions presented by Guillain, Barré, and Strohl have withstood the test of time. Their landmark publication has become a standard of excellence in the history of clinical neurology. Deservedly, "GBS" is one of the most recognized medical eponyms around the world.

INTRODUCTION

In 2016 we observed the 100th anniversary of the seminal publication by Georges Guillain, Jean-Alexandre Barré, and André Strohl, which led to a definition of one of the most recognized clinical syndromes in the history of neurology.[1,2] Their report included superb longitudinal clinical observations of progressive areflexic paralysis in 2 patients, unique laboratory findings from lumbar puncture, and electrophysiological observations with a novel myographic study of tendon reflexes.

Of the 3 authors, two were neurologists (Guillain and Barré).[3,4] During World War I, Guillain was director of the Neurological Services for the Sixth French Army. After the war, he was appointed Professor of Diseases of the Nervous System and held the position of the Charcot Chair at the Salpêtrière Hospital in Paris between 1923 and 1948. He was a prolific writer and lecturer, and made many contributions to clinical neurology; however, despite his significant body of work, with multiple publications on various neurological topics, his legacy has been defined by the work on a syndrome described in the 1916 publication.

Barré did part of his neurological training with Joseph Babinski. During World War I, he worked with Guillain in the Sixth French Army neurological unit. He authored and coauthored several hundred papers and was a professor of neurology in Strassbourg.[3]

Strohl (Figure 1) was the youngest of the 3 authors. During World War I, among other medical duties, he performed radiological exams. He typically is credited for performing the myographic studies of tendon reflexes, one of the hallmarks of the 1916 paper. Unfortunately, he was later not given the appropriate credit for his work, and the classic eponym does not include his name. Nevertheless, after World War I he had a very successful medical career. He was interested in physiology and was professor of physiological medicine in Algiers and later in Paris. At the very young age of 35, he was elected to the Académie de Médecine.[5,6]

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REVIEW AND DISCUSSION

The 1916 article was not the first report of progressive areflexic paralysis in the medical literature. Spreading paralyses had been observed and reported for many years prior.[7,8] The most frequently quoted is the classic report of ascending paralysis by Landry in 1859.[9,10] The case of a 43-year-old patient, from the first part of Landry's report, was very well documented by detailed longitudinal observations and examinations. Any physician practicing today would have no difficulty recognizing many of the characteristic features of what we now refer to as a Guillain-Barré syndrome (GBS). Guillain had difficulty accepting Landry's index case—and other similar cases—as representing the same syndrome he and his colleagues reported in 1916. He made several arguments in speeches and subsequent publications on the differences between his classic observations and case reports by other authors.[11,12] One of the major differences Guillain pointed out was that the prognosis in the syndrome he described was typically good, whereas Landry's index patient had died. However, Landry's case report was very valuable because it also provided autopsy findings showing, most importantly, that the spinal cord was not affected. One can only speculate that the prestige of having an eponym linked exclusively to his own publication is what drove Guillain to dismiss not only Landry's report, but also many other similar cases reported prior to 1916, as belonging to the same syndrome he described. Nevertheless, to this day some neurologists refer to cases of areflexic paralysis caused by polyradiculoneuritis as a Landry-Guillain-Barré-Strohl syndrome.[7]

Why was the 1916 publication so important, and why has it had such a widespread impact on the practice of clinical neurology? There are 3 major elements that make that publication such a classic. First, it is an excellent demonstration of diligent clinical neurological examination, performed in a longitudinal fashion, allowing neuroanatomical localization of the neurological deficit within the peripheral nervous system. Second, the clinical investigations incorporated the still new at that time technique of lumbar puncture (introduced by Quincke in 1891)[13] into the diagnostic process, which led to the discovery of the characteristic cerebrospinal fluid (CSF) abnormalities. Third, the authors introduced a novel study of tendon reflexes with a myographic method, which improved the understanding of the underlying neuropathophysiology of the paralysis and complemented the clinical exam. That work eventually led to recognition of the clinical utility of electrodiagnositc techniques in evaluation of patients with neuromuscular diseases.

The authors' clinical excellence is evident from reading the diligent, thorough description of findings from longitudinal neurological examinations of their patients. By 1916, the bedside techniques of comprehensive neurological examination were well established.[14] Trained neurologists had a good understanding of neuroanatomy, and usually, with a high degree of confidence, were able to recognize upper motor versus lower motor neuron causes of weakness. The two cases described in the 1916 publication were French soldiers, infantry men, age 25 and 35. The clinical presentation was strikingly similar in both patients and can be summarized by the following: (1) progressive weakness of all limbs, initially starting with difficulty marching, affecting the distal muscle more than proximal; (2) loss of tendon reflexes; (3) preservation of cutaneous reflexes; (4) paresthesia; (5) some mild objective sensory loss; (6) severe muscle tenderness on palpation; (7) no sphincter incontinence; and 8) good recovery.

It is not clear why the authors decided to perform the lumbar puncture on their 2 patients. It is probable that they wanted to rule out any possible infectious process, including polio. Or perhaps they were merely tempted to utilize a novel, exciting diagnostic tool that could possibly provide some additional information about the etiology of the neurological syndrome they observed. Whatever their rationale, their observation of the albumino-cytologic dissociation (ACD) has been one of the all-time most important findings in the diagnosis of GBS. The authors wrote in their paper that the same spinal fluid abnormality had been previously observed in cases of cord compression, Pott's disease, and neurosyphilis. However, they accurately claimed that it had previously never been reported in cases of pure radiculitis or polyneuritis. A century later, the ACD is still one of the most important laboratory findings in evaluation of patients with suspected GBS. Of course, in clinically typical cases today, an expert clinician would never rule out the GBS diagnosis based on the normal CSF protein content, which may vary over the

Figure 1. Dr. André Strohl

Portrait of Professor André Strohl by L. De Fleurac. Published in 1928 in Chanteclair. Collection of the Bibliothèque interuniversitaire de Santé. From reference 5. Public domain.

Figure 2. The Myographic Curve

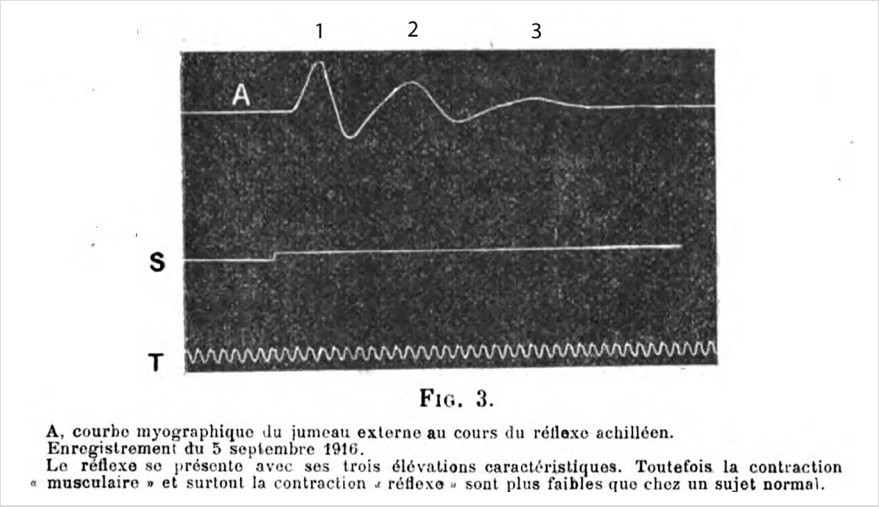

FIG. 3.

A, courbe myographique du jumeau externe au cours du réflexe achilléen. Enregistrement du 5 septembre 1916. Le réflexe se présente avec ses trois élévations caractéristiques. Toutefois la contraction « musculaire » et surtout la contraction « réflexe » sont plus faibles que chez un sujet normal.

One of the 3 figures from the 1916 paper. The myographic curve was recorded from the lateral gastrocnemius muscle after percussion of the Achilles tendon. The figure shows 3 characteristic elevations which, according to the authors, represented: (1) mechanical jerk caused by impact of the percussion hammer, (2) "muscular" (idiomuscular) contraction, and (3) the "reflex" muscle contraction with the longest latency. The authors commented that the registered "muscular" and especially the "reflex" contractions were very weak compared to a normal subject. From reference 1 (numbers indicating specific elevations of the myographic curve were added by the author).

course of the disease and, even in classic cases, the ACD may not be observed.[15] On the other hand, the finding of the characteristic CSF abnormalities is very reassuring for a clinician evaluating a patient with suspected GBS. Guillain himself insisted that the very high CSF protein is almost a sine qua non diagnostic finding in GBS and had reservations in recognizing many of the reported cases where the CSF protein was not markedly elevated.[11]

There has been some misunderstanding about the type of electrophysiologic studies that were conducted and described in the 1916 paper. The authors reported that the excitability of different muscles and nerves to galvanic and faradic stimulations was mostly preserved, although some responses were attenuated and some muscles and nerve trunks were slightly hyperexcitable. Those techniques were not novel and already had been in use by physicians in the second half of the 19th century, even without good understanding of the underlying neurophysiological phenomena.[16] However, the novelty of the 1916 report was the original report on the myographic method to study the abnormalities of tendon reflexes in the course of the disease in the first of the 2 described patients. The authors mention that the timing of the muscle tendon excitation was registered with the help of the apparatus referred to as a "signal de Desprez".[17] They recorded the latencies from the moment of tendon percussion to the onset of muscle contraction. They indicated that typically (in normal subjects) 3 different elevations were observed in the myographic curves, corresponding to: (1) mechanical jerk, (2) "muscle" (likely idiomuscular) contraction, and (3) "reflex" contraction (Figure 2). They observed that the latencies of the "reflex" muscle contraction waves were markedly delayed or nonrecordable at different stages of the disease and later the responses reoccurred, correlating with clinical improvement. The registered "muscle" (idiomuscular) contractions also were attenuated and delayed but were better preserved than the "reflex" muscle contractions. The findings from the myographic study of the tendon reflexes led the authors to conclude that the likely pathophysiology was related to the disruption of the central part of the reflex arc. The role of myelin in nerve physiology, and its importance for saltatory nerve conduction, was still unknown in 1916.[18] Electrophysiological studies over the next decades clearly demonstrated that the primary pathology in most cases of GBS is nerve demyelination, frequently associated with early loss of tendon reflexes. The pioneering myographic study reported in 1916 heralded future incorporation of modern electrophysiological tests to evaluations of patients with suspected GBS and other neuromuscular conditions. The authors rightly recognized the importance of the myographic technique as complementing the clinical exam.

Despite Strohl's major contributions to the 1916 report, his name eventually was dropped from the eponym. Draganesco and Claudian usually have been credited for introducing the eponym of the Guillain-Barré syndrome, dropping Strohl's name in 1927.[19] There are several possible explanations for the omission of Strohl's name from the eponym. Strohl was not a neurologist and was very young at the time of the 1916 publication, thus likely not respected by the contemporary neurologists. Also, it seems that Guillain himself, in his multiple public speeches and subsequent articles, did not consistently mention Strohl's name when referring to their work.[4,7] There was also speculation that there might have been some political reason for not giving Strohl the credit he deserved. Strohl not only had a German last name, but was born in Alsace, a heavily German province in France, suggesting that he may have been a victim of anti-German sentiments after World War I.[20] One might also presume that the eponyms with 3 names are not "user friendly" because they are simply too long.

Our understanding and definition of the GBS has evolved since the initial description in 1916, representing its expanding clinicopathological spectrum.[21] There is an ongoing dispute over how broadly the spectrum of the GBS can be expanded before the eponym could lose its meaning and nosological specificity. Should it be reserved to cases with predominantly demyelinating pathology? Should terms such as "pure sensory" or "autonomic" variants of GBS be used? There will always be splitters and lumpers, and the controversy will continue.

The seminal observations and most of the conclusions presented by Guillain, Barré, and Strohl have withstood the test of time. Their publication has become a landmark and standard of excellence in the history of clinical neurology. Deservedly, "GBS" is one of the most recognized medical eponyms around the world.

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