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History of Neurology

Charles-Jacob Marchal de Calvi (1815–1873), description of arteriopathy and diabetic neuropathy

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INFO ARTICLE

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ABSTRACT

Charles-Jacob Marchal (1815–1873) was a physician from Calvi in Corsica who is today unjustly forgotten. Among his numerous publications, his 1864 book, *Recherches sur les accidents diabétiques et essai d'une théorie générale du diabète* (Research on diabetic problems and an attempt at a general theory of diabetes), is noteworthy. It compiles several of his earlier works on diabetes, with the addition of texts by English and German authors made available to him through the work of Jean-Martin Charcot (1825–1893) and his translations. In this book, Marchal demonstrated that diabetes caused gangrene in the lower limbs, and numerous severe infections, rather than being caused by these pathologies, as had been previously thought. He showed that the arterial calcifications that caused arterial thrombosis and the sensory disturbances indicating diabetic neuropathy were the consequences of the prolonged and often silent progression of diabetes. As such, he was a pioneer in these areas. Marchal's work deserves to be remembered because of this epistemological breakthrough, amounting to a paradigm shift, which the American philosopher and science historian Thomas Kuhn (1922–1996) described in 1962 as the motor of progress in scientific knowledge.

During his Tuesday Lesson on 13 December 1887 [1], Jean-Martin Charcot (1825–1893) lectured his students on the symptomatology of ''intermittent claudication'' in diabetics. He extended his scope to neurological complications in diabetes, noting, ''The history of this neuropathy was sketched out from 1848 to 1850 by Marchal de Calvi. It was unknown up to that point but has become significantly more complicated since then.'' After a brief historical overview of the knowledge on diabetes and a short biographical note on Marchal, we will examine the seminal descriptions he left us with, notably in his book *Recherches sur les accidents diabétiques et essai d'une théorie générale du diabète* (Research on diabetic problems and an attempt at a general theory of diabetes), published in 1864 [2].

1. History of knowledge on diabetes: a summary

Diabetes is a metabolic pathology mainly affecting carbohydrates and lipids. It is characterised by persistent hyperglycaemia resulting from deficient secretion or action of

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insulin or both. Knowledge of diabetes dates back to ancient times. Egyptian papyruses, Indian and Chinese texts, and works by Greek and Arab physicians attest to the tasting of urine in patients with unrelenting thirst; the taste of the urine in these cases was compared to honey [3]. In the second century AD, Aretaeus de Cappadoce coined the word ''diabetes'' (from the Greek διαβαινω/*diabaino*, to move through, as in the case of fluids) and established the disease's clinical picture to include thirst, polyuria, and emaciation [4]. Thomas Willis (1621–1675) added ''mellitus'' to take account of the sugary taste of the urine. One of Marchal's contemporaries, Claude Bernard (1813–1878), established the first pathophysiology of the regulation of glycaemia, notably by seeing the liver as the ''organism's great laboratory''. Convinced of the pre-eminent role of the autonomic nervous system in regulating metabolism, he initially believed he had discovered the cause of diabetes by inducing hyperglycaemia with an injection to the ''floor of the cerebellar ventricle above the origin of the vagus nerves'' (4th ventricle) [5–7]. In 1848, Bernard wrote, ''The formation of sugar in the liver, which is clearly a chemical fact, is directly related to the influence of the nervous system'' [8]. An entire generation of clinicians would pursue this dead end of seeking the cerebral origin of diabetes before the role of the pancreas was brought to light. Take, for example, the work of Théodore Émile Leudet (1831–1922) in 1857, which he entitled, *Influence des maladies cérébrales sur la production du diabète sucré* (Influence of cerebral diseases on the production of diabetes mellitus), and which reported cases of hemiplegia with the presence of urinary sugar [9]. Leudet saw diabetes as merely a complication of neurological damage. Several decades later, in 1947, the Nobel Prize in Medicine was awarded to the Argentinian Bernardo Alberto Houssay (1887–1971) for his work on the endocrine physiology of the pituitary gland. He showed that pseudo-diabetes by injection results from a stimulation of the medulloadrenal complex and is unrelated to true diabetes [10].

Marchal immediately criticised the impact of experimental studies such as the ''diabetic injection'' and publications such as that of Leudet: ''These results must not be superposed on medical facts or, even worse, be used to confiscate them, as it is clear that productive cerebrospinal lesions have prevented physicians from recognising produced cerebrospinal lesions'' [2]. He thus clearly expressed the fact that diabetes is the cause of vascular and nervous lesions, and that diabetes is not cerebral in origin.

For several centuries, diabetes was recognised by the thirst and polyuria it caused but also by the ''saccharine'' deposit, identified by taste, that remained after the evaporation of urine. During the period in which Marchal was working, the detection of glucose in urine confirmed the diagnosis of diabetes, but in a crude and subjective way, relying solely on the visual assessment of colour. Since 1849, pharmacists had been using Fehling's solution [11] (or that of Bareswill), composed of copper sulphate and potassium tartrate. In the solution, initially blue, a dark red deposit forms (copper salts) after boiling, and only in the presence of a compound with an aldehyde functional group, such as reducing sugars like glucose, galactose, or maltose. The darker the red, the higher the quantity of glucose [12]. We now know that glucosuria may be absent as diabetes progresses.

2. Biographical note

Born on 03 July 1815 in Calvi, where his father, a military officer, resided, Charles-Jacob Marchal studied in Bastia, his mother's native city (Fig. 1). On 27 June 1831, he moved in with his sister and her husband, an accountant at the Hospital of Alger, one year after the city had been conquered. He was only 16 but was put to work as a surgeon's assistant. After three years in Algeria, he passed a competitive exam enabling him in 1833 to start work at the Val de Grâce, advanced training hospital in Paris, while pursuing his studies at the medical school. He defended his thesis on 12 June 1837 before a jury presided by Alfred Velpeau (1795–1867): *Nouveaux procédés de ligature des artères poplitée et axillaire* (New ligation procedures for popliteal and axillary arteries) [13]. By then a military *aide-major* surgeon, he made an unsuccessful attempt at the *agrégation* exam (which opens the way to an academic career) in 1839 with a thesis entitled *Des bourses synoviales et de leurs maladies* (Synovial bursas and their diseases) [14]. He collaborated on publications for Velpeau's journal, *Annales de la chirurgie française et étrangère*, and for that of Casimir Broussais (1803–1847), *Recueil des mémoires de médecine et de chirurgie militaires*. He passed the *agrégation* exam in 1844, defending a thesis entitled *Des abcès phlegmoneux intra-pelviens* (Intrapelvian phlegmonous abscesses) [15]. In 1845, he was given the position of professor of anatomy and physiology at the Val de Grâce School. On 06 May 1846, he was made a Knight of the French Legion of Honour [16]. He took part in the Revolution of 1848 but failed in his bid to be elected as a national assembly deputy (Fig. 2).

He was also unsuccessful at the 1850 competitive exam at the medical school for the Chair of Hygiene. In 1852, Marchal decided against continuing his military career when he

Fig. 1 – Monument to Charles Marchal – Boulevard Wilson – Calvi (© e-monumen.net).

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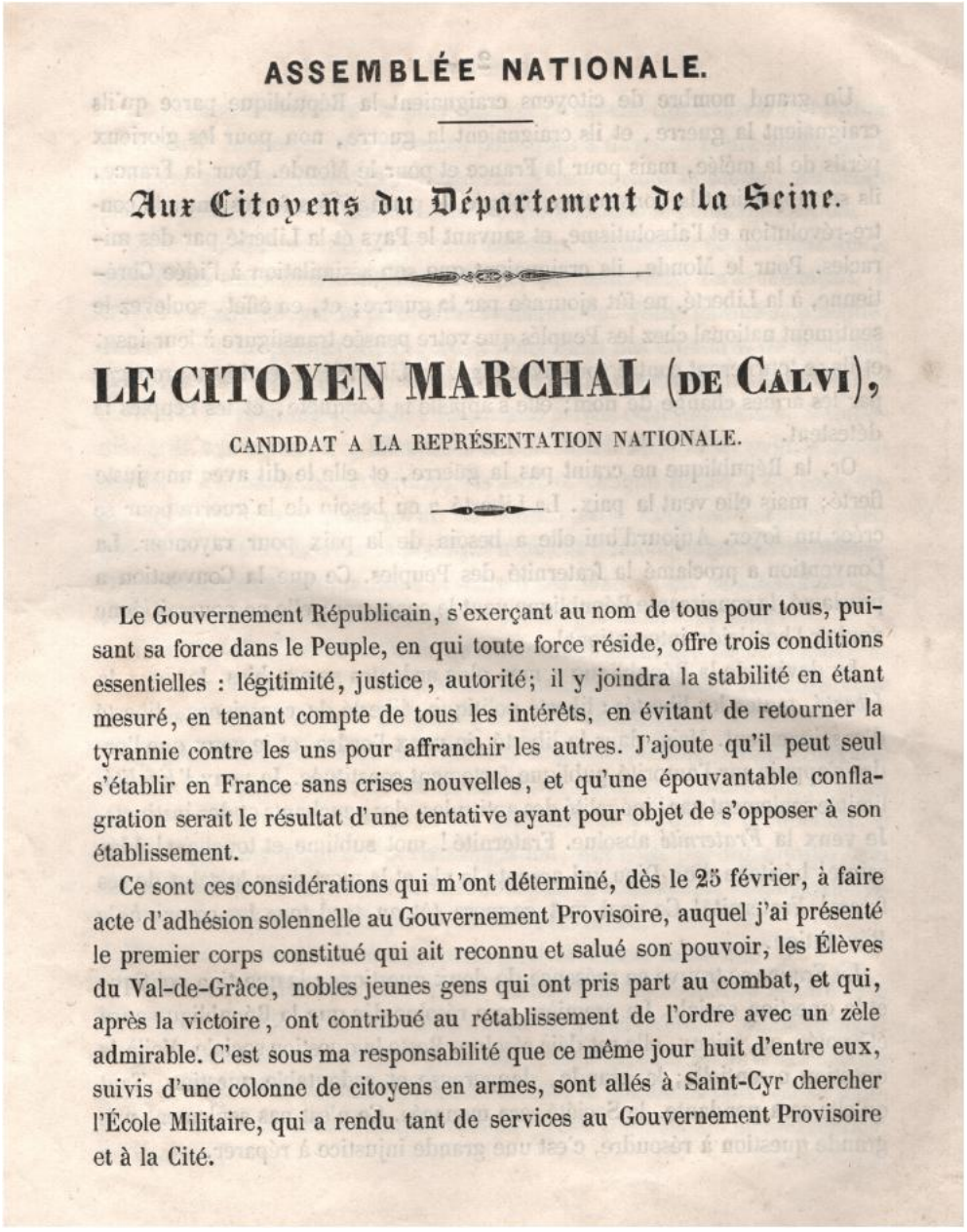

ASSEMBLÉE NATIONALE.

Aux Citoyens du Département de la Seine.

LE CITOYEN MARCHAL (DE CALVI),

CANDIDAT A LA REPRÉSENTATION NATIONALE.

Le Gouvernement Républicain, s'exerçant au nom de tous pour tous, puisant sa force dans le Peuple, en qui toute force réside, offre trois conditions essentielles : légitimité, justice, autorité; il y joindra la stabilité en étant mesuré, en tenant compte de tous les intérêts, en évitant de retourner la tyrannie contre les uns pour affranchir les autres. J'ajoute qu'il peut seul s'établir en France sans crises nouvelles, et qu'une épouvantable conflagration serait le résultat d'une tentative ayant pour objet de s'opposer à son établissement.

Ce sont ces considérations qui m'ont déterminé, dès le 25 février, à faire acte d'adhésion solennelle au Gouvernement Provisoire, auquel j'ai présenté le premier corps constitué qui ait reconnu et salué son pouvoir, les Élèves du Val-de-Grâce, nobles jeunes gens qui ont pris part au combat, et qui, après la victoire, ont contribué au rétablissement de l'ordre avec un zèle admirable. C'est sous ma responsabilité que ce même jour huit d'entre eux, suivis d'une colonne de citoyens en armes, sont allés à Saint-Cyr chercher l'École Militaire, qui a rendu tant de services au Gouvernement Provisoire et à la Cité.

Fig. 2 – Citizen Marchal presenting his views for the national assembly elections on 23 April 1848 (Collection OW).

learned he would be sent to Algeria. He instead developed a large private clientele, no longer working as a surgeon but as a physician. He published numerous short works, founded the journal *La Réforme médicale* in 1867, which became *La Tribune médicale* in 1869 and remained in existence until 1936. Known for his melodious and vibrant voice, he was recognised as an excellent orator, debater, and polemicist. Following heart failure, he died of cerebral haemorrhage on 24 February 1873 at only 57 years old [17].

Marchal de Calvi wrote extensively on subjects as varied as preventive recommendations for socialites [18], the effects of introducing air into veins [19], angina resulting from diphtheria or scarlet fever (to oppose the cauterisation of pseudomembranes on the tonsils) [20], and poisoning by turpentine.

3. Diabetic gangrene

In his presentation on the complications of diabetes on 25 November 1856 at the French Academy of Sciences, Marchal asserted he was the first, on 13 April 1852 [21], to attribute to diabetes the cause of gangrene in the lower limb of a patient [22]: "Before 1852, no one imagined that diabetic gangrene might exist" [2]. His book, published in 1864 (Fig. 3), was based on 133 cases, including personal cases and those found in the

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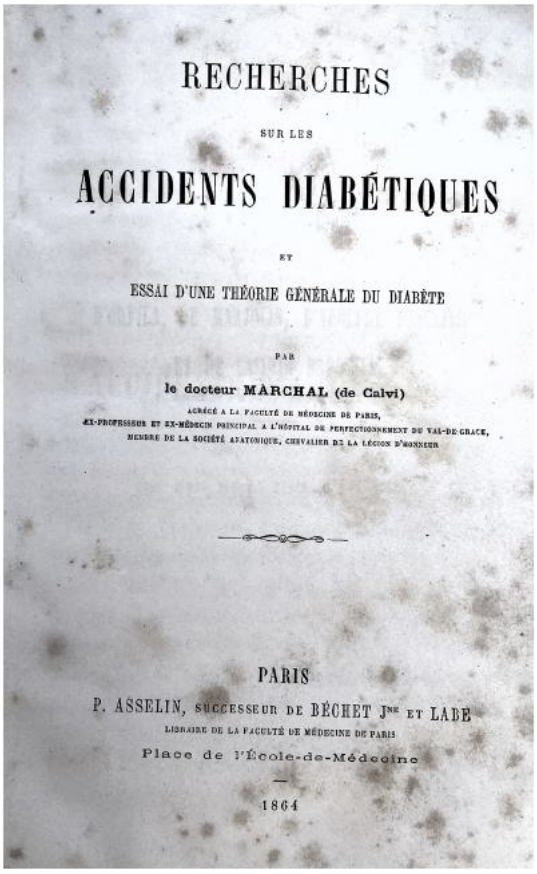
RECHERCHES
SUR LES
ACCIDENTS DIABÉTIQUES
ET
ESSAI D'UNE THÉORIE GÉNÉRALE DU DIABÈTE
PAR
le docteur MARCHAL (de Calvi)
AGRÉGÉ A LA FACULTÉ DE MÉDECINE DE PARIS,
EX-PROFESSEUR ET EX-MÉDECIN PRINCIPAL A L'HÔPITAL DE PERFECTIONNEMENT DU VAL-DE-GRACE,
MEMBRE DE LA SOCIÉTÉ ANATOMIQUE, CHEVALIER DE LA LÉGION D'HONNEUR
PARIS
P. ASSELIN, SUCCESSEUR DE BÉCHET JNE ET LABÉ
LIBRAIRE DE LA FACULTÉ DE MÉDECINE DE PARIS
Place de l'École-de-Médecine
1864

Fig. 3 – Cover of Marchal de Calvi's book (OW Collection).

French and English literature [2]. All the following citations are taken from this book.

Marchal contested the results of physiology experiments that succeeded in triggering diabetes through action on the central nervous system, without naming Bernard. Thereafter, Marchal relied solely on clinical medicine, at the patient's bedside, and on the accumulation of observations to advance his concept of diabetes and its complications: ''Diabetes creates a tendency toward inflammation and gangrene'', but he did recognise that ''we do not know the nature of the state that, in diabetes, leads to inflammation and gangrene in the tissues, but regarding its effects, we are entirely certain in confirming its existence''. He put forward a pathophysiological hypothesis: ''We can only deduce from this state that sugar circulates in pure form in the vessels, constantly infusing the tissues and acting on vital solids so as to excite them and weaken them, to incite them to fight and to disarm them''. In addition: ''The presence of sugar in the blood creates an inflammatory diathesis in the internal membrane of the capillary vessels, a diathesis whose manifestations, other than simple rashes, arise with a gangrenous tendency due to the profound debility in which diabetes immerses the organism''. He did not fail to highlight the insidious nature of the disease: ''The frequency of diabetes [is] much greater than we have ever assumed it to be; it is surprisingly easy for physicians to fail to recognise it, given both to the relative frequency of latent diabetes and patients' lack of awareness'' [2]. Moreover: ''Many individuals are diabetic and have been for a number of years, without any reason to suspect it, given that the ordinary signs of diabetes are not present''.

He thus rejected ''the expression 'senile gangrene'' with ''its negative influence on the question of gangrene in general. It has prolonged confusion and error by leading one to think that any form of spontaneous gangrene in the extremities is due to arterial blockage, especially ossification, and it has always been inaccurate because, as a matter of principle, it has been recognised that often so-called senile gangrene may occur well before senility.'' Without citing Rudolph Virchow (1821–1902), Marchal explicitly established the arterial origin of gangrene: ''An intra-arterial clot blocks blood flow, whether this clot was formed by embolism, or produced following inflammation of the internal membrane of the vessel, which I believe to be infinitely more common''. He also established this dogma: ''While every diabetic is exposed to gangrene, in every individual with so-called spontaneous gangrene, we must suspect the existence of diabetes and immediately set out to confirm it''.

Starting in 1861 [23], Marchal explained that most physicians practising in his day thought gangrene caused diabetes, or that boils, carbuncles, and other abscesses caused glycosuria. Take, for example, the observation presented in 1861 by Jean-Marie Philipeaux (1809–1892) and Alfred Vulpian (1826–1887), ''A case of transient diabetes that occurred during the development of a carbuncle'' [24]. Marchal did not fail to highlight the fact that glycosuria may be absent while diabetes is in fact progressing and has been for some time. He also asserted that when faced with any outbreak of pustules or boils or with any pruriginous vulvar erythema, diabetes must be looked for immediately, even though the idea of microbial or mycotic infection was not available to him at that time. His book contains numerous long discussions of infections based on their location that are no longer relevant. We now know that an acute infection can destabilise treated diabetes, but this has nothing in common with the cases presented by Marchal. For the record, the link between diabetes and pruritis, notably genital pruritis, was established by Victor Alban Fauconneau-Dufresne (1798–1885) in 1858 [25].

In 1853, Marchal presented to the French Academy of Sciences an observation of ''amaurotic paraplegia'', a condition he attributed to diabetes [26]: ''It may be possible that diabetes produces paraplegia in the same way it produces amaurosis; it then becomes essential to examine the urine of both paraplegics and amaurotics'' [27]. He also presented various clinical cases of apoplexy that he attributed to diabetes. For example, a patient died of cerebral apoplexy after gangrene in his toes: ''I see no reason not to attribute the cerebral lesion to the same diathesis that produced gangrene in the toes''. Marchal was thus the first to posit a causal link between diabetes and gangrene and between diabetes and hemiplegia or the loss of vision. He added: ''It is essential to examine the urine of individuals complaining of habitual fatigue and weakening in the lower extremities''. He was looking for ''a significant decrease in sensitivity and heat, and later, the paleness and cooling of the foot can be noted'', or ''tingling, anaesthesia, or disturbances in tactility''. One of his examples illustrates peripheral neuropathy: ''A Creole friend

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of mine, who was accustomed to eating, after his dinner, a handful of pieces of cane sugar, felt extreme weakening in his lower extremities with tingling in his feet''. It must be recognised that Marchal did not explicitly distinguish between the role of nervous system damage and arterial deficit, even though he noted cases of ''aberrant sensitivity in the soles of the feet''. While Marshall Hall (1790–1857) had proposed the notion of reflex in 1833, Marchal's clinical examination did not yet include the routine of checking tendon reflexes [28].

Marchal's reasoning, whereby diabetes is the cause and not the consequence, perfectly illustrates the concept of a ''paradigm shift'' introduced in 1962 by the American philosopher and science historian Thomas Kuhn (1922–1996). The sciences do not progress continually, but rather through breakthroughs that change paradigms [29] (*Weltanschauung* in German).

In his book, Marchal added another observation: the increased frequency in diabetics of the ''invincible retraction of flexor tendons'' in the hand; that is, the disease described by Guillaume Dupuytren (1777–1835) in 1831 [30]. He also did not fail to mention that ''the reduction or even the total elimination of the virile force is closely linked to the disease'' (he also used the term ''radical force''). He recognised Thomas Hodgkin (1798–1866) as the first to describe impotence in diabetic men in 1854, as well as kidney damage [31]. It should be remembered that Hodgkin also showed improvement in diabetes with physical exercise, an idea introduced in France by Apollinaire Bouchardat in 1851 [32].

4. Charcot's contribution and discussion

It is impossible to conclude without noting that Charcot, from the time of his residency with Pierre Rayer (1793–1867), took an interest in the same subject as Marchal. With his knowledge of English and German, he unearthed forgotten authors who had already established a link between carbuncles and diabetes, but initially Marchal was unaware of them [33]. Charcot wrote: ''Based on the documents before us, it seems clear that diabetic gangrene was seen in England well before 1852, in a more pronounced way than Mr. Marchal believed. It was seen in its three main forms: gangrene that is senile in appearance, gangrenous phlegmons, and gangrenous carbuncles'' [34]. Charcot presented observations from the Scottish Andrew Duncan (1773–1828) [35], the German Philipp Friedrich Wilhelm Vogt (1787–1861) [36], and the Englishmen William Cheselden (1688–1752) [37], John Latham (1761–1843) [38], and William Prout (1785–1850) [39]. In 1861, Charcot did not fully share Marchal's views on shifting the pathophysiological paradigm: ''Interpreting these kinds of facts is quite difficult, if not nearly impossible, in the current state of science. Relative to diabetes, do carbuncles act as an excitatory cause by provoking some reflex action? Or are they produced under the influence of the same organic disturbance that tends to develop an excess of sugar in the economy? Or are carbuncles a direct consequence of the sudden appearance of sugar in the blood, and thereafter, in the tissues?... Empirical observation taken alone is still imperfect and, consequently, any serious attempt at an explanation would be, for the time being, clearly premature''. In his 1864 book, Marchal thanked Charcot for his historical contribution. He examined the writings of each of the authors cited by Charcot in an attempt to demonstrate that none of them had explicitly shifted the paradigm; that is, by positing diabetes as the cause and not the consequence. In his 1878 *Exposé des titres scientifiques* (Presentation of scientific titles), Charcot wrote only one line, without comments, on his work on the history of diabetic gangrene. Charcot's clear interest in the study of diabetes has also gone unmentioned by his foremost biographers [40].

5. Conclusion

It seems unfair that Charles-Jacob Marchal de Calvi has been forgotten. Starting in 1853, the acuity of his observations and his thinking made it possible for him to invalidate a theory considered well established, namely that gangrene, abscesses, carbuncles, and other outbreaks were the cause of diabetes. Marchal called for considering diabetes as the cause of these pathologies, notably arterial gangrene by thrombosis at the calcifications in arterial walls, and motor deficits with paraesthesia in the lower limbs, or diabetic neuropathy. This epistemological breakthrough owing to a paradigm shift perfectly illustrates the philosophy of progress in scientific knowledge, developed in 1962 by the American philosopher and science historian Thomas Kuhn.

Statement of ethics

This work required no approval from an institutional review board and was prepared in accordance with the ethical guidelines of the journal *La Revue Neurologique*.

Disclosure of interest

The author declares that he has no competing interest.

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