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History of Neurology

Adolphe Gubler (1821–1879) or Parisian neurology outside La Salpêtrière in the age of Jean-Martin Charcot

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INFO ARTICLE

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ABSTRACT

Adolphe Gubler (1821–1879) is a typical example of a 19th century hospital physician in Paris. Head of a medical unit at Beaujon hospital in 1855, he was nominated to the treatment and pharmacognosia Chair in 1868. He trained many students who became his disciples and remained very close to him. Gubler published prolifically in all areas of medicine. His most well-known work is clearly his contribution to the study of vascular accidents affecting the brain stem, which Auguste Millard worked on simultaneously; hence the eponymous Millard-Gubler syndrome, an example of crossed hemiplegia. Following a brief biography, we will present Gubler's main publications in the area of neurology: on migraine, neurological damage during acute rheumatic fever, aphasia, and the autonomic nervous system. Much of this work was carried out through student theses that Gubler directed. The fame of his contemporary Jean-Martin Charcot (1825–1893) eclipsed that of Gubler, even though the latter was well known and respected among Parisian professors. By tying together the diverse threads of his work, we hope to renew interest in this 19th century neurologist.

The eponymous Millard-Gubler syndrome is familiar to neurologists [1]. In 1856, Auguste Millard (1830–1915), who was still an *interne* or a medical student living and working in the Paris hospitals, wrote a report on the presentation that his colleague Hippolyte Sénac (1830–1892) gave to the members of the *Société Anatomique*. Drawing on the cases reported in the 1851 thesis of Pierre-Henri Josias (1825–1895) [2], Sénac gave a complete clinical picture of crossed hemiplegia. Apparently unaware of this work, Adolphe Gubler (1821–1879) also defined in 1856 "crossed paralysis, this singular variety of hemiplegia in which the face is paralysed on one side, while the limbs are paralysed on the opposite side" [3]. In this first publication, Gubler deduced "probable damage of the pons" because "the facial nerves that project to the pons are already crossed, whereas the tracts that project to the limbs are not yet crossed". He provided other clinical and anatomopathological evidence for this localization in a second publication in 1859 [4,5]. Gubler officially accepted sharing credit for this first description with Millard in a letter sent to the journal, as demanded by Millard! [6].

Following a brief biography of Gubler, we will show how he used his observational skills as an expert clinician to study the many facets of neurology, resulting in a wide range of publications, especially as evidenced by the theses of his students.

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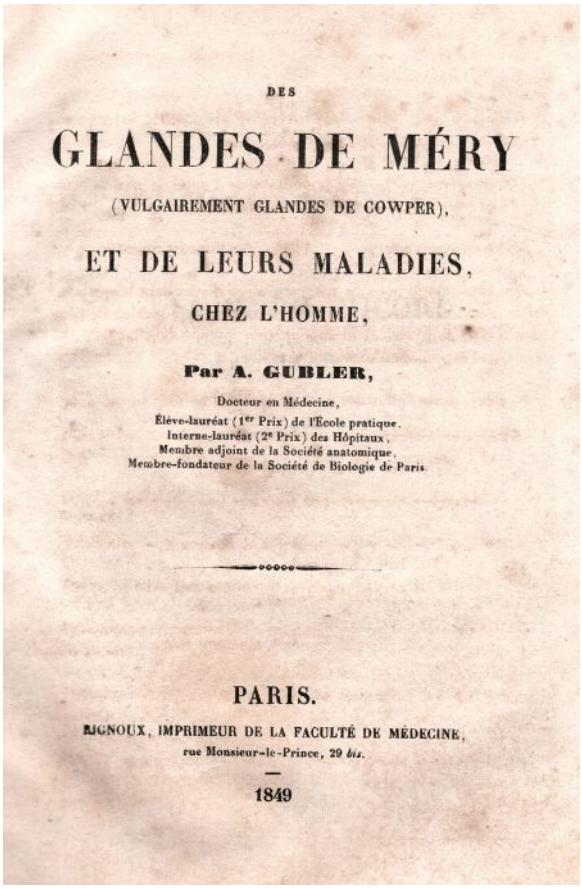
Fig. 1 – Adolphe Gubler. In Dr. A. Corlieu, Centenaire de la Faculté de Médecine 1794–1894. Alcan et al., 1895. (Private collection of the author).

1. A biography

Adolphe (Nicolas, Marie) Goblet, who went by the name Adolphe Gubler, was born on 5 April 1821 in Metz in Northeast France. His father had died before his birth, and his mother, unable to provide for his upbringing, sent the young Adolphe to her sister in Rocroy in Northern France. There Gubler was a brilliant student throughout his primary and secondary studies, with a particular liking for classical texts which he read fluently in both Latin and Greek. But his true passion, from childhood, was the study of plants which he collected during walks through the countryside with his uncle, who had been a military pharmacist. Proud of his herbarium which he had patiently classified, he went so far as to attempt the beginnings of a new classification system! Once he had obtained both the scientific and literary baccalaureates, he enrolled at the *Faculté de Médecine* in Paris, ''full of enthusiasm but with meager funds'' [7]. In 1844, Gubler was an *externe*, ''non-residential student'', and worked under Armand Trousseau (1801–1867), who admired his botanical knowledge. To assist Gubler financially, Trousseau helped him obtain a position to accompany a rich young ''melancholic'' on a voyage to Switzerland and Italy, with the aim of improving the patient's mood. One night in Milan, Gubler's charge, overcome with hallucinations and delusions of persecution, shot at Gubler then tried to stab him. The bullet that lodged in his thorax was not removed. Later, ''he quite often described a pain in his side and would say: 'I can feel my bullet'''. His face, neck, and chest were lacerated, leaving scars which he always tried to cover by wearing his hair long and with sideburns (Figs. 1 and 2) [7]. This serious accident did not prevent him from passing his first attempt at the 1845 competitive exam to become an *interne*, ''full-time resident'', in the Paris hospitals. In 1849, Gubler defended his thesis: *Des glandes de Méry (vulgairement glandes de Cooper) et de leurs maladies chez l'homme* (Méry glands (commonly known as Cooper glands) and their diseases in man) (Fig. 3). He then served under Jean-Baptiste Bouillaud (1796–1881) as *chef de clinique* (or chief *interne*) and soon thereafter passed his first attempt at the competitive exam to become a hospital physician [8]. Advancing swiftly, Gubler went on to enter the university phase of his career by passing the *agrégation* exam in 1853: ''Among his first works,

Fig. 2 – Adolphe Gubler surrounded by his students at Beaujon hospital in 1877. (Private collection of the author).


DES

GLANDES DE MÉRY

(VULGAIREMENT GLANDES DE COWPER),

ET DE LEURS MALADIES,

CHEZ L'HOMME,

Par A. GUBLER,

Docteur en Médecine,
Élève-lauréat (1er Prix) de l'École pratique,
Interne-lauréat (2e Prix) des Hôpitaux,
Membre adjoint de la Société anatomique,
Membre-fondateur de la Société de Biologie de Paris.

PARIS.

RIGNOUX, IMPRIMEUR DE LA FACULTÉ DE MÉDECINE,
rue Monsieur-le-Prince, 29 bis.

1849

Fig. 3 – Cover of Adolphe Gubler's thesis, defended in 1849. (Private collection of the author).

one of the most important was undoubtedly his agrégation thesis on cirrhosis, a thesis still considered classical in that it contains the most exact description of the anatomical lesions caused by this disease, as well as the most rational explanation of the metamorphoses that the cirrhotic liver undergoes'' (Fig. 4) [7,9].

On 28 July 1856, Gubler married Jeanne-Hélène David d'Angers (1836–1926), the daughter of the sculptor Pierre-Jean David d'Angers (1788–1856); they would have one daughter. Gubler spent most of his hospital career at Beaujon Hospital, where he taught courses in medical pathology. After replacing Gabriel Andral (1797–1876), who held the Chair of General Pathology and Treatment, in 1858 and 1859, Gubler succeeded Germain Sée (1818–1896) in 1868, thereafter holding the Chair of Treatment and Pharmacognosia at the *Faculté de Médecine*. ''Gubler was a man of learned societies; he assiduously attended sessions and contributed the fruit of his labours'' [10]. Gubler was vice-president of the *Société de Biologie* in 1852, after serving as one of the society's founding members in 1848. He was also vice-president of the *Société de Botanique* from 1862 to 1866. ''Once he had founded his theories, he cherished them as one does children. He defended them fervently, and almost always with success''. In 1865, he was elected a member of the *Académie de Médecine* in the ''treatment and medical natural history'' section. Gubler founded the *Journal de Thérapeutique* in 1874, published by Georges Masson (1839–1900), which remained in print after Gubler's death until 1883 [6]. And on 11 September 1865, he was awarded the *Chevalier de la Légion d'honneur* medal [11].

''The memory of his difficulties as a young man made Gubler particularly compassionate toward struggling young students, and we now know, from at least some of those who haven't forgotten, that he helped more than one student avoid the deprivations he himself had suffered'' [6]. Every Friday evening, Gubler and his friends gathered for urbane diners. His closest and most faithful friend was Alexandre Bonnefin (1832–1911); amongst the others were Hermann Pidoux (1808–1882), Jules Cloquet (1790–1883), and Henri Bouley (1814–1885). In 1874, Gubler bought Cloquet's property in the Lamalgue district of Toulon (Southeast France), where a hotel now stands, on rue Gubler. On 20 April 1879, Gubler died in Toulon of stomach cancer, at age 58 [7,8,12].

The most significant of Gubler's many and varied non-neurological contributions include his description of liver damage in syphilitic new-borns, the ''*signe de la pommette*'' (during pneumonia, cheekbone redness is indicative of the side of pulmonary damage), isolation of herpes esophagitis, introduction of the therapeutic use of jaborandi, rationalization of the use of potassium bromide, refutation of homeopathy [13], definition of physiochemical acid conditions favouring the spread of oral thrush, and research on proteinuria which he considered to be a symptom and not a disease. ''He was one of the first to use microscopes for clinical work'', which led him to describe, among other things, ''epithelial cell casts, granular casts, and hyaline casts in urine'' [7,8]. Gubler began to preside over the juries for his doctoral students in 1869. Their thesis subjects covered all aspects of medicine.

2. Error of an *interne* who went on to fame: Octave Landry

Octave Landry (1826–1865), who passed the *internat* competitive examination in 1849, worked as an *interne* under Gubler in 1853 [14]. The previous year, he had published an article entitled *''Recherches physiologiques et pathologiques sur les sensations tactiles''* (Physiological and pathological research on tactile sensations). In it, he wrote: ''Temperature sensations are distinct from and independent of touch and pain'' [15]. In 1855, he was the first to develop the concept of ''the sensation of muscular action''—that is, the concept of proprioception and stereognosis, based on observations gathered in the departments of Gubler at Beaujon Hospital and Claude-Stanislas Sandras (1802–1856) at the Hôtel Dieu Hospital [16].

Of note among the questions posed by the jury, listed in the back of Landry's thesis, is a pathological anatomy question concerning: ''Apoplexy of the pons and the spinal cord'' [17]. There is no way of knowing Landry's response on the day of his defence, but in his *Traité complet des paralysies* published in 1859, he contested the theory proposed by his thesis director, Gubler, in 1853: ''Mr. Gubler's position, perfectly plausible, assumes scientific backing for a highly contestable assertion: the decussation of nerve roots themselves''. Landry was wrong; his error lay in considering the pons to be specifically a

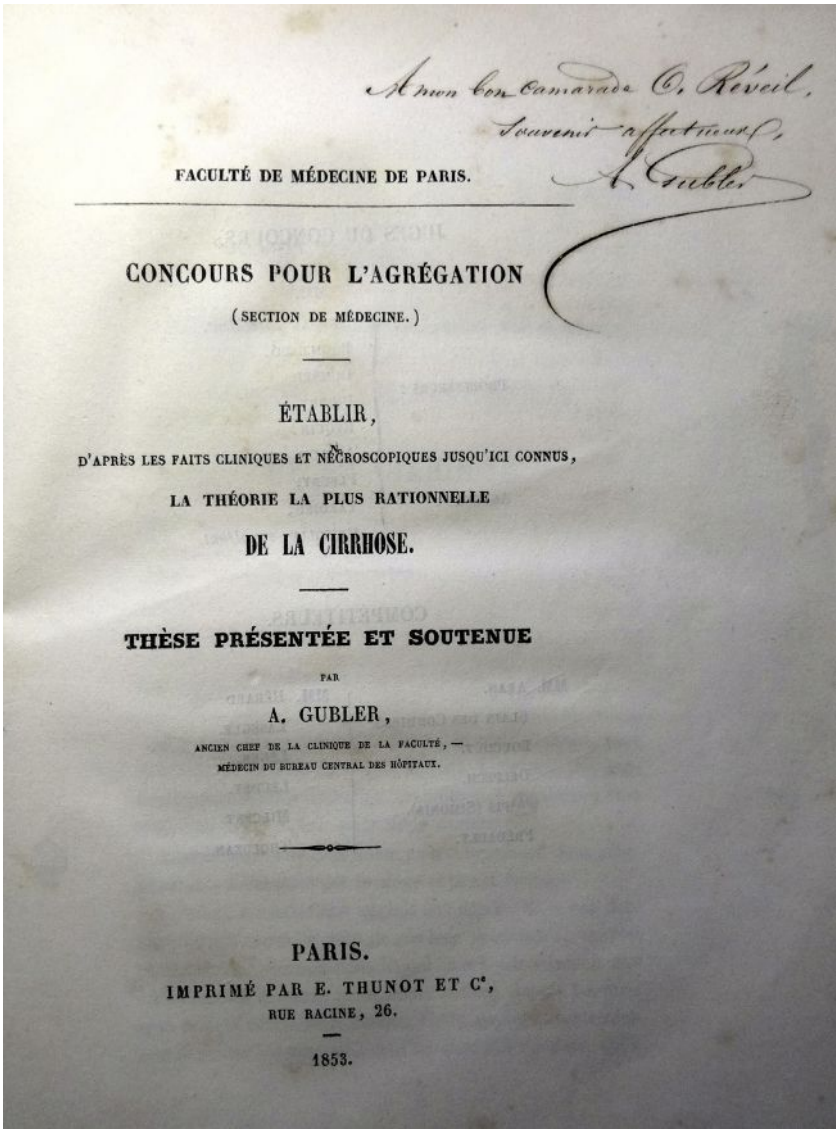
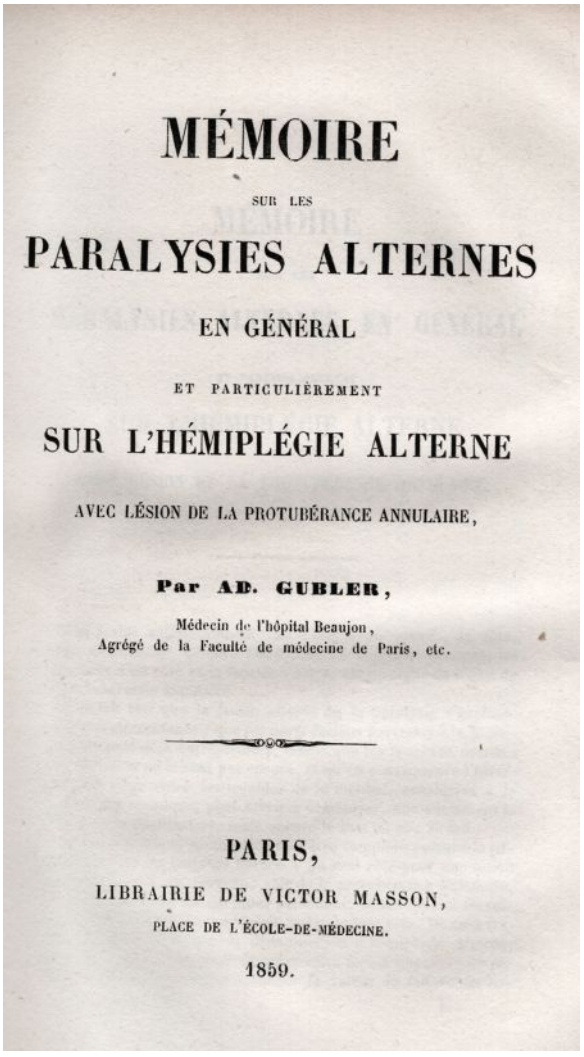


Fig. 4 – Adolphe Gubler's *agrégation* thesis dedicated to Pierre-Oscar Réveil (1821–1885). (Private collection of the author).

centre of motion and sensation and in being unaware of the existence of a corticobulbar tract: ''As a means of transmission, the mesencephalon extends its influence throughout the body; but, as a motor and sensory centre, its influence is limited to the organs to which it projects nerves [. . .]. We now understand why damage to the pons always results in crossed hemiplegia in the limbs and trunk, whereas for the face it sometimes leads to crossed hemiplegia, sometimes to ipsilateral weakness or hemiplegia''. Gubler, on the other hand, had the prescience to assert: ''The originating fibres of facial nerves cross at certain points along their path and, for example, the nerve that emerges on the left side of the pons originates on the right side of the encephalon, or at least derives its motor function there'' (Figs. 5 and 6). In neither of these two publications did Gubler refer to paralysis of ocular motion.

As noted by Félix Féréol (1825–1891) [18], the credit ''for having studied and interpreted ocular deviation'' — that is, paralysis of the laterality of vision associated with crossed hemiplegia — should be attributed to Achille Louis Foville or Defoville (1831–1887) (Fig. 7). Foville had noted: ''The decussation of the roots of the facial nerve has been established beyond doubt by Mr. Vulpian and Mr. Philipeaux through their important work on the origins of the cranial nerves'' [19]. Jean-Marie Philipeaux (1809–1892) was an assistant to the holder of the Chair of Comparative Physiology Pierre Flourens (1794–1867) at the *Muséum d'Histoire Naturelle* in Paris. With Alfred Vulpian (1826–1887), he had indeed published, in 1853: ''*Essai sur l'origine de plusieurs paires des nerfs crâniens*'' (Essay on the origin of several pairs of cranial nerves), which was the commercial edition of Vulpian's thesis [20]. In his 26 July 1864 lesson, Vulpian gave an accurate report of semiology and anatomopathology of facial paralysis by localization of an ischaemic accident in the pons [21]. Féréol would be the first to give the anatomoclinical demonstration of the connections between the nuclei of the third and sixth cranial nerves, which



MÉMOIRE

SUR LES

PARALYSIES ALTERNES

EN GÉNÉRAL

ET PARTICULIÈREMENT

SUR L'HÉMIPLÉGIE ALTERNE

AVEC LÉSION DE LA PROTUBÉRANCE ANNULAIRE,

Par AD. GUBLER,

Médecin de l'hôpital Beaujon,
Agrégé de la Faculté de médecine de Paris, etc.

PARIS,

LIBRAIRIE DE VICTOR MASSON,

PLACE DE L'ÉCOLE-DE-MÉDECINE.

1859.

Fig. 5 – *Mémoire sur les paralysies alternes* (Dissertation on crossed paralysis), Adolphe Gubler 1859. (Private collection of the author).

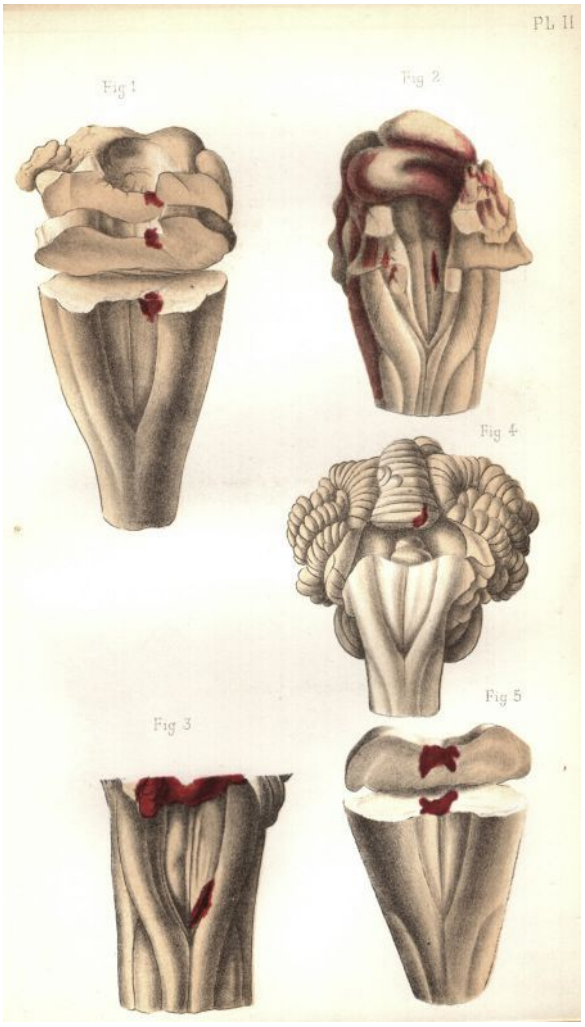


Fig. 6 – Plate illustrating the thesis of Gaston Graux (1848–1925) in 1878. *Contribution à l'étude des localisations cérébrales (mésencéphale) : de la paralysie du moteur oculaire externe avec déviation conjugée (paralysie centrale par lésion du noyau de la 6e paire)* (Contribution to the study of cerebral localizations (mesencephalon): external ocular motor paralysis with conjugal deviation (central paralysis by damage to the nucleus of the sixth cranial nerve)). (Private collection of the author).

Foville had only suspected [22]. Féréol's student Gaston Graux (1848–1825) would make this the subject of his thesis in 1878 (Fig. 6) [23]. The anatomical and experimental research of Graux would be confirmed by Jean-Baptiste Vincent Laborde (1830–1903) and Mathias Duval (1844–1907) in 1880 [24].

Gubler directed and presided over the theses of three of his students who had studied crossed paralysis. In 1847, Victor Fontorbe (1850–1901) described an aneurysm in the right vertebral artery compressing the pons which in turn caused left hemianaesthesia with right facial paralysis, but the association with middle cerebral artery thrombosis may have also explained the left hemiplegia [25]. In 1876, Victor Schoepfer (1851–?) reported a case of complete hemiplegia with anaesthesia, remarkable due to the appearance of hemiataxia during regression of the motor deficit indicating damage to the middle cerebellar peduncle at the base of the pons [26]. In 1877, Léon Feuillet (1852–?) sought to ''establish that hemianaesthesia originating in the mesencephalon could be real, complete, and comparable in intensity to cases of cerebral hemianaesthesia'' associated with crossed hemiplegia as described by Gubler.

3. Jérémie Girard and "cerebral rheumatism"

Bouillaud described ''rheumatic endocarditis'', that is, heart damage during acute rheumatic fever, in 1840 [27]. Germain Sée (1818–1896) wrote in 1850: ''Rheumatism frequently affects the nervous system, resembling in its characteristics neuroses or simulating phenomena, either isolated or grouped, of

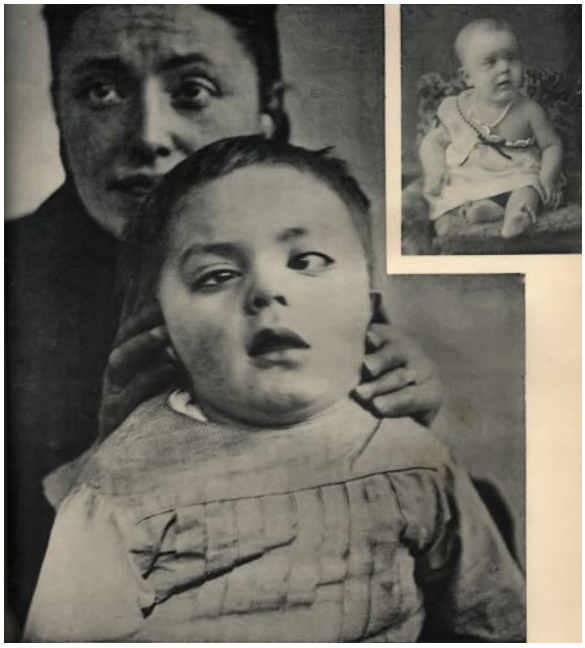


Fig. 7 – « *Un cas d'hémiplégie alterne compliqué de strabisme interne bilatéral et de glossoplégie* » (A case of crossed hemiplegia complicated by bilateral internal strabismus and glossoplegia), Achille Souques, Nouvelle Iconographie de La Salpêtrière 1891;4:358-361. (Private collection of the author).

diseases of the encephalon, the spinal cord, or their envelopes [28]. The example given by Sée, which his student Jacques-Pierre Botrel (1819–?) revisited in his thesis [29], was the chorea they had been the first to associate with acute rheumatic fever: ''Chorea is the result of rheumatic diathesis and results in plastic inflammation of the heart membranes, meninges, pleura, and peritoneum with or without rheumatic fever''.

Paying homage to his mentor Bouillaud, Gubler extended the scope of this type of pathology in 1857: ''Ingenious observers have shown us that rheumatism attacks by turns the various serous membranes as well as the articular capsules, and it affects the various viscera involved'' [30]. Gubler's in-depth historical research led him to conclude that ''the phenomena remain the same; only the interpretations have varied, depending on the physician's point of view, and on the state of science in the country and period of each physician''; he then proposed various observations to demonstrate that in addition to chorea, other types of neurological damage were associated with acute rheumatic fever. For him, ''une céphalalgie de forme gravitive'' (that is, a serious, severe headache that worsens when the head is moved forward or back) could inaugurate the fever. Momentary delirium or meningoencephalitis may also be linked to rheumatism: ''As a cause, rheumatism often impacts the heart during generalized acute rheumatic fever, and endocarditis is the rule. Consequently, why not recognize that cerebral accidents, much more exceptional in fact, occur in the same way?'' He nonetheless refuted the existence of ''rheumatic apoplexy''. His pathophysiological explanation is hypothetical: ''The causal action of rheumatism appears to involve the serovascular envelope of the encephalon, this latter ordinarily becoming the point of inflammation, but consecutively the cortical substance participates in the inflammation'' [30]. His student Jérémie Girard (1835–?), confronted with cases of rapid death and unable to find macroscopic traces of cerebral lesions, provided a prescient and clear-sighted explanation that is also elegantly phrased: ''We have no shame admitting that when the scalpel fails in the search for lesions in an illness clearly observed, the organic damage, invisible to our eye, is entirely interior and in this way molecular'' [31]. Benjamin Ball (1833–1893) was inspired by the writings of Gubler and by Girard's thesis for his own agrégation thesis defended on 14 March 1866: Du rhumatisme viscéral [32].

4. Ulysse Bailly and paralysis in various diseases

Alfred Maingault (1823–1884) defended his thesis on 11 August 1854 entitled *La paralysie du voile du palais à la suite d'angine* (Paralysis of the soft palate following angin [33], with Achille-Pierre Requin (1803–1854) presiding over the jury. Maingault identified diphtheria, described by Pierre Bretonneau in 1826 [34], as the cause of paralysis. Inspired by this, Gubler collected over several years cases of acute illness accompanied by paralysis, either in the acute phase or during convalescence. This explains his statement that ''I engaged Dr. Landry to carefully gather and promptly publish such cases of ascending paralysis, which he had studied especially, but also to provide important evidence supporting my proposition''; said proposition being that ''generalized paralysis may follow on from a series of acute illnesses, not only those that are virulent or septic such as cholera, dysentery, typhoid fever, and eruptive fevers, but also those that are clearly inflammatory, such as tonsillar angina, herpetic tonsillitis, and pneumonia'' [35]. Gubler surveyed all of these pathologies using numerous clinical cases. Eruptive fever (measles, scarlet fever, smallpox, erysipelas) and typhoid fever may be followed by ''general paralysis'', ''general anaesthesia'', or convulsions, but the cause, according to Gubler, could not be assessed during the anatomopathological exam. ''Encephalitis may be the site of prolonged functional disturbance, even when what can be called the molecular modifications of the substance cannot be detected by current means of investigation, which means that paralysis can exist without noticeable (detectable) cerebral lesion. He sometimes observed abnormal movements, such as ''a strange play of sudden, disorderly, choreoid, contractions throughout much of the body'', for which he mentioned a possible cerebellar cause, with reference to recent experiments by Flourens on the role of the cerebellum in movement control. Gubler sought to avoid an over-simplification popular in his day, which involved diagnosing diphtheria as soon as paralysis appeared during fever.

On 11 January 1872, Gubler presided over the jury for the thesis of his *externe* Ulysse Bailly (1846–1909) [36]. Bailly added several observations in order to support the theory of his teacher but, more specifically, he reported on the anatomopathological discoveries published by Jean-Martin Charcot (1825–1893) and Vulpian in 1863 [37] — peripheral nerve damage in the absence of muscular damage during diphtheria — as an

argument for the theory defended by Gubler. This type of neurological pathology would not be explained until the discoveries of Louis Pasteur (1822–1895), then the notion of bacterial toxins, followed by the emergence of immunology.

We should credit Gubler with helping to list and identify this type of pathology, but also with allowing Landry to isolate ''acute ascending paralysis'' [38], before such pathologies were re-evaluated in 1879 by Jules Dejerine (1849–1917) in his thesis [39], and in 1916 by Georges Guillain (1876–1961) and Alexandre Barré (1880–1967), under the eponymous name still in use today, Guillain-Barré syndrome [40].

5. Arthur Bordier (1841–1910) and migraine

In 1873, Amédée Dechambre (1812–1886) asked Gubler and Arthur Bordier (1841–1910), his *interne,* to write the migraine entry in the *Dictionnaire Encyclopédique des Sciences Médicales*. After a description of migraine that might easily be found in a publication today with no need for revision, Gubler recalled that Pierre-Adolphe Piorry (1794–1879) [41] had ''insisted on a particular form of the condition (irisalgic migraine) in which optical disturbance is particularly intense; a cloud seems to appear in the centre of the image rubbed off on the retina, followed by the appearance of luminous arcs around a darkened point, and on this point there are zigzagging lines of fire that produce continual scintillation''. The accuracy of this description is in fact based on self-observation by Piorry [42]. Gubler did not omit any of the clinical aspects, neither susceptibility to odours, nor vomiting, nor the relief brought by sleep, nor factors favouring the disturbance, nor the favourable prognosis, etc. He surveyed the diverse pathophysiological opinions offered at that time, and proposed, presciently, that: ''Trigeminal involvement seems incontestable.'' For Gubler, relief could most often be obtained from opium, rest, and darkness. And he concluded that the physician ''can take heart in the fact of at least providing some relief, even if he is not always able to cure''.

6. Arthur Bordier and ''vasomotor nerves''

In 1868, the thesis of Bordier, dedicated to Gubler but presided over by Alexandre Axenfeld (1825–1876), reviewed knowledge about the physiological role of the ''ganglionic nervous system'', that is, the autonomic nervous system, by its sympathetic component, as it was understood at the time following the work of Claude Bernard (1813–1878). Bordier referenced the strange theory of Gubler: ''The sympathetic nervous system is a sort of condenser that receives the energy given off by respiratory combustion and transmits it to centres of innervation. When it acts in this manner, the vessels are contracted and there is little heat. On the other hand, when it stops drawing the energy for chemical actions from the vessels, calorification intensifies and the capillaries release'' [43]. Bordier cited, as an example of the ganglionic nervous system, cheekbone redness during pneumonia, a sign described by Gubler [44]. At the end of Bordier lengthy thesis, he attempted to list the medications modulating sympathetic action, such as opium, belladonna, rye ergot; he also noted the indications, referring each time to examples from the teachings of Gubler [45].

7. Alcide Rontin (1844–1903) and aphasia

After working under Gubler as a temporary *interne*, Alcide Rontin (1844–1903) defended the opinion of Gubler in his 1873 thesis, which was based in part on the theories of Pierre Gratiolet (1815–1865) and on Trousseau's lessons. He admitted that ''when I was an interne I borrowed from him [Gubler] some of my most curious clinical thinking'' [46]. Then he noted straightaway that aphasia was a symptom and not a disease: ''We will adopt the opinion of Bouillaud, who places the coordinating centre of thought, the legislative power of speech in the anterior lobes of the brain''.

After analysing the writings of Paul Broca (1824–1880) [47,48] and Adrien Proust (1834–1903) [49], and essentially rejecting them, Rotin put forward the opinion of Gubler: ''If the damage in aphasia is almost always located on the left, this is because of a sort of pathological selection of which we present numerous clinical examples. Who is unaware of the fact that nine times out of ten intercostal neuralgia affects the left side? And doesn't rheumatism, as established by Bouillaud, affect almost exclusively the left part of the heart? He localized ''intelligence and memory in the anterior lobes''. According to Gubler, speech also depended on the ''medulla oblongata'', the location of the ''system of execution''. For Gubler and Rontin, aphasia ''is linked to a lesion either in the anterior lobes or in transmission fibres or in the system of execution'', and amnesia ''is one of its forms''. As for the aetiology, ''all of the causes that disturb encephalic circulation and damage brain substance at one or several of its points, may produce aphasia''. Gubler's thinking on aphasia was not carried forward by anyone. His anatomopathological bases are poorly established, as Rontin's reading indicates. The distinction between thought and language is clear and varies according to the examples used. Finally, Gubler's absence from the sessions of the *Société d'Anthropologie*, where the productive discussions between Gratiolet, Ernest Auburtin (1825–1893, Bouillaud's son-in-law), and Broca took place, meant that Gubler's ''most curious'' ideas based on approximative physiology were excluded straightaway [50].

8. Lucien de Valicourt (1853–1920) and hemiplegia observed during pleurisy

The pathophysiology of thrombosis and embolism was a frequently debated subject at the beginning of the 19th century. The first thesis mentioning inflammation and intracardiac blood stasis as factors favouring the formation of a clot was defended by Charlemagne Legroux (1798–1861) in 1827 [51]. During a discussion at the *La Société médicale des Hôpitaux*, Gubler spoke of ''erratic blockages'' in 1857 to refer to a migrating or embolic clot [52]. This idea was revisited by his student Lucien de Valicourt de Séranvilliers (1853–1920) [53]; Gubler presided over the jury for Valicourt de Séranvilliers's thesis on 8 November 1875. Gubler's student included a few hemiplegia observations during infectious pleurisy. He pro-

posed an embolic mechanism causing middle cerebral artery thrombosis starting with pulmonary vein thrombosis compressed by significant pleural effusion and/or neighbouring pleural inflammation. He suspected, and rightly so, the cause to be a modification of blood coagulability arising from the inflammatory condition, favouring clot formation, and calling to mind the thesis of Legroux. He also suggested that Gubler would have referred to ''erratic blockages'' before the work of Rudolph Virchow published in 1856 [54]: ''It was only thereafter that Virchow, according to the Germans, gave science a new doctrine, a theory resting mainly on his bibliographic and experimental research''. In fact, it is impossible to establish any sort of anteriority based on any specific publication by Gubler.

9. Homage paid by Charcot

When Charcot gave his lessons on Parkinson's disease, he insisted on the differential diagnosis between shaking at rest and shaking in action. He recognized that only Gubler had accurately interpreted the phenomenon, as early as 1860: ''The shaking does not consist in a succession of contrary movements outside of wilful control, but rather as alternating contraction and release of the muscles that are involved'' [55].

10. Posterity and fame

In 1878, Léon Ginain (1825–1898) was the architect in charge of enlarging, on the rue Hautefeuille side, the old *Faculté de Médecine* in Paris, which had been built from 1774 to 1786 under the direction of Jacques Gondouin de Folleville (1737–1818) [56]. To honour the solemnity of the central stairway and the main hall leading to the lecture halls, Ginain had a bust of a former professor placed on each of the pilasters [57]. Next to the busts of Gabriel Andral (1797–1876) or Jean-Baptiste Bouillaud (1796–1881), for example, the bust of Adolphe Gubler (Fig. 8) attests to the esteem his colleagues had for him and their posthumous acknowledgement of his work, which they wished to commemorate lastingly in 1900. For over a century, thousands of students have passed by without noticing, illustrating the precept of Alexandre Vialatte (1901–1971): ''Statues merely point toward forgetting; one is never deader than when rendered in bronze''. It must be realized that, despite Gubler's numerous works, only the eponymous Millard-Gubler syndrome commemorates him, and does so almost exclusively among neurologists.

Charcot taught anatomopathology at the *Faculté de Médicine* from 1872 to 1882. Most of his teaching was conducted at the La Salpêtrière Hospital which undoubtedly explains the absence of a bust at the medical school. His legitimate glory and international renown result from his isolation and description of neurological diseases such as multiple sclerosis, Parkinson's disease, and amyotrophic lateral sclerosis. The publications Gubler left us cannot rival Charcot's. But as a good instructor, Gubler formed several generations of practitioners of family medicine, covering almost all medical fields. This is the highly honourable mission of a medical school professor, and Gubler fulfilled it perfectly.

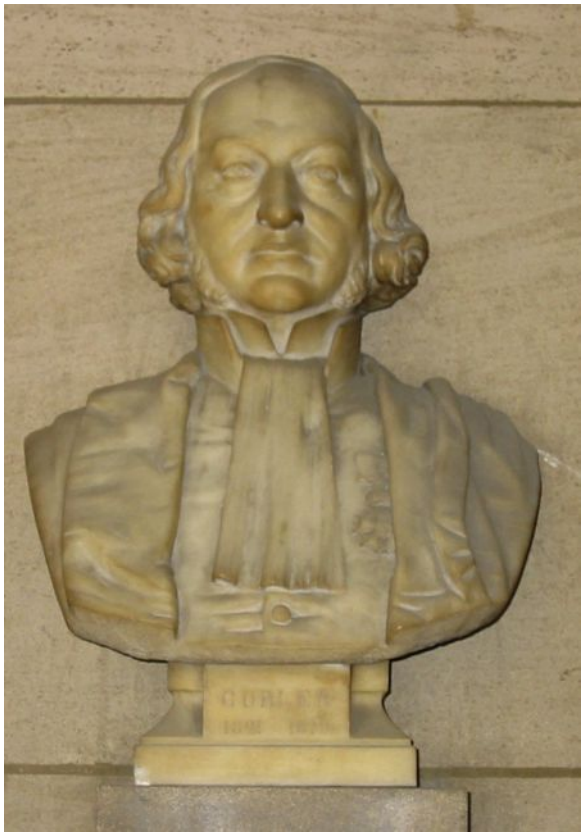


Fig. 8 – Adolphe Gubler's bust in the main hall of the *Faculté de Médecine* in Paris, rue de l'École de Médecine. (Photographed by the author).

Disclosure of interest

The author declares that he has no competing interest.

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REFERENCES

[1] Silverman IE, Liu GT, Volpe NJ, Galetta SL. The crossed paralyses. The original brain-stem syndromes of Millard-Gubler, Foville, Weber, and Raymond-Cestan. Arch Neurol 1995;52(6):635–8.
[2] Josias PH. Des hémorrhagies de la protubérance annulaire ou mésocéphale. Rignoux; 1851, Thèse Paris n° 162: imp..
[3] Cenac H, Millard A. Hémorrhagie de la protubérance annulaire. Bull Soc Anat Paris 1856;36:206–21.
[4] Gubler A. De l'hémiplégie alterne envisagée comme signe de lésion de la protubérance annulaire et comme preuve de la décussation. Gaz Hebd Med Chirur 1856;3(43):749–54 [(45):789-792 / (46):811-816].
[5] Gubler A. Mémoire sur les paralysies alternes en général, et particulièrement sur l'hémiplégie alterne, avec lésion de la

protubérance annulaire. Gaz Hebd Med Chir 1858;5(42):721–3 [(45):765-769 / (47):801-804 / (52):883-886 / 1859;6(1):3-7 / (4):52-55 / (6):86-90].
[6] Millard A. Correspondance : à Monsieur le rédacteur en chef de la Gazette Hebdomadaire. Gaz Hebd Med Chirur 1856;3(46):816–8.
[7] Bergeron J. Eloge de M. Gubler. Mem Acad Med 1899;38:1–28.
[8] Gubler A. Notice sur les titres et travaux scientifiques. Paris: Imprimerie et librairie administrative de Paul Dupont; 1876
[9] Gubler A. Établir, d'après les faits cliniques et nécroscopiques jusqu'ici connus, la théorie la plus rationnelle de la cirrhose. Thèse d'agrégation. Paris: E. Thunot et Cie; 1853.
[10] Paul C. Notice sur M. Adolphe Gubler. Union Med 1879;28(77):8–20 [3e série].
[11] Archives nationales, base Léonore, dossier LH1214011.
[12] His widow remarries in 1881with Paul Leferme (1823–1899), Inspecteur général des Ponts et Chaussées, in charges of ligfthouses and beacons.
[13] Gubler A. Leçon Clinique sur l'homéopathie. Gaz Hôpitaux civils et militaires 1871;44(149):590–1 [(150):597-599].
[14] Walusinski O. Pioneering the concepts of stereognosis and polyradiculoneuritis: Octave Landry (1826–1865). Eur Neurol 2013;70(5–6):281–90.
[15] Landry O. Recherches physiologiques et pathologiques sur les sensations tactiles. Arch Gen Med 1852;4(29):257–75 [1852;4(30)28–56].
[16] Landry O. Mémoire sur la paralysie du sentiment d'activité musculaire. Paris: Typographie Henri Plon; 1855.
[17] Landry O. Considérations générales sur la pathogénie et les indications curatives des maladies nerveuses. Rignoux; 1854, Thèse Paris n°321: imp..
[18] Poirier J. Le docteur Félix Féréol, 1825–1891 : avocat, médecin, artiste. Paris: Hermann; 2015.
[19] Foville A. Note sur une paralysie peu connue de certains muscles de l'œil, et sa liaison avec quelques points de l'anatomie et la physiologie de la protubérance annulaire. Bull Societe Anat Paris 1858;33:393–414.
[20] Philipeaux MM, Vulpian A. Essai sur l'origine de plusieurs paries des nerfs crâniens, 3e, 4e, 5e, 6e, 7e, 8e, 9e et 10e. Paris: Rignoux; 1853.
[21] Vulpian A. Leçons sur la physiologie générale et comparée du système nerveux faites au Museum d'Histoire Naturelle. Paris: Germer Baillière; 1866.
[22] Féréol F. Note sur la communication anatomique existant entre les noyaux d'origine de la troisième et de la sixième paire. Bull Mem Soc Med Hop 1873;9:370–4.
[23] Graux G. Contribution à l'étude des localisations cérébrales (mésencéphale), de la paralysie du moteur oculaire externe avec déviation conjuguée (paralysie centrale par lésion du noyau de la 6e paire). JB. Baillière; 1878, Thèse Paris n° 383.
[24] Duval M, Laborde JBV. De l'innervation des mouvements associés des globes oculaires. Etudes d'anatomie et de physiologie expérimentale. Journal de l'anatomie et de la physiologie normales et pathologiques de l'homme et des animaux 1880;16:56–89.
[25] Fontorb V. Un cas d'hémiplégie alterne par anévrysme de la vertébrale. A. Parent; 1874, Thèse Paris n° 313.
[26] Schoepfer V. Considérations sur un cas d'hémianesthésie avec mouvements ataxiques succédant à une hémiplégie du même côté. A. Parent; 1876, Thèse Paris n° 271.
[27] Bouillaud JB. Traité clinique du rhumatisme articulaire et de la loi de coïncidence des inflammations du cœur avec cette maladie. Paris, Londres: J.-B. Baillière; 1840.
[28] Sée G. De la chorée, rapports du rhumatisme et des maladies du cœur avec les affections nerveuses convulsives. Memoires de l'Academie Imperiale de Medecine 1850;15:374–525.
[29] Botrel JP. De la chorée considérée comme une affection rhumatismale. imp. Rignoux; 1850, Thèse Paris n° 79.
[30] Gubler A. Etudes et observations cliniques sur le rhumatisme cérébral. Arch Gen Med 1857;Ve série 9:257–85.
[31] Girard EJ. Essai sur le rhumatisme viscéral. imp. Rignoux; 1862, Thèse Paris n° 19.
[32] Ball B. Du rhumatisme viscéral. Paris: P. Asselin; 1866.
[33] Maingault VPA. De la paralysie du voile du palais à la suite d'angine. imp. Rignoux; 1854, Thèse Paris n° 194.
[34] Bretonneau PF. Des inflammations spéciales du tissu muqueux et en particulier de la diphtérie, ou inflammation pelliculaire, connue sous le nom de croup, d'angine maligne, d'angine gangreneuse. Paris: Crevot; 1826.
[35] Gubler A. Des paralysies dans leurs rapports avec les maladies aiguës, et spécialement des paralysies asthéniques, diffuses, des convalescents. Mémoire lu à la Société médicale des hôpitaux, le 14 décembre 1859. Archives générales de Médecine 1860;série 5(15):257-272/402-421/534-551/693-713/1860; série 5(16):187-202/718-742/1861;série 5(17)306-366.
[36] Bailly U. Des paralysies consécutives à quelques maladies aiguës. imp. Parent; 1872, Thèse Paris n° 19.
[37] Charcot JM, Vulpian A. Note sur l'état des muscles et des nerfs du voile du palais dans un cas d'angine diphtérique. C R Seances Soc Biol 1863;3è série 4:173–6.
[38] Landry O. Note sur la paralysie ascendante aiguë. Gaz Hebd Med Chirur 1859;6(30):472–4 [et 1859;6(31):486-488, accompagnée d'une note de Gubler].
[39] Dejerine J. Recherches sur les lésions du système nerveux dans la paralysie ascendante aigue. Versailles: imp. Cerf; 1879, Thèse Paris n° 81.
[40] Guillain G, Barré JA, Strohl A. Sur un syndrome de radiculonévrite avec hyperalbuminose du liquide céphalo-rachidien sans réaction cellulaire. Remarques sur les caractères cliniques et graphiques des réflexes tendineux. Bull Mem Soc Med Hop 1916;40:1462–70.
[41] Piorry PA. Mémoire sur l'une des affections désignées sous le nom de migraine ou hémicrânie. In: Du procédé opératoire à suivre dans l'exploration des organes par la percussion médiate, et Collection de mémoires sur la physiologie, la pathologie et le diagnostic. Paris: JB. Baillière; 1831
[42] Lardreau E. La migraine, biographie d'une maladie. Paris: Les Belles Lettres; 2014.
[43] Bordier A. Des nerfs vaso-moteurs ganglionnaires, anatomie, physiologie, pathologie, thérapeutique. A. Parent; 1868, Thèse Paris n° 72.
[44] Gubler A. De la Rougeur des pommettes comme signe d'inflammation pulmonaire, mémoire lu à la Société médicale des hôpitaux de Paris. Union Med 1857;11(49):199–201 [(51):209-210 / (53):215-216].
[45] Gubler A. Commentaires thérapeutiques du Codex medicamentarius ou Histoire de l'action physiologique et des effets thérapeutiques des médicaments inscrits dans la Pharmacopée française. Paris: JB. Baillière; 1868.
[46] Rontin A. Quelques considérations sur l'aphasie. F. Pichon; 1873, Thèse Paris n° 209.
[47] Broca P. Perte de la parole, ramollissement chronique et destruction partielle du lobe antérieur gauche du cerveau. Séance du 18 avril 1861. Bulletin de la société française d'anthropologie 1861; 2:235-238/Localisation des fonctions cérébrales, siège du langage articulé, séance du 16 avril 1863. Bulletin de la Société française d'Anthropologie 1863; 4:200-204.
[48] Broca P. Remarques sur le siège de la faculté du langage articulé, suivies d'une observation d'aphémie (perte de la parole). Bull Soc Anat Paris 1861;6:330–57.
[49] Proust A. De l'aphasie. Arch Gen Med 1872;6è série 19:147–66 [303-318 / 653-685].

[50] Messerli P. Une approche historique de l'aphasie. In: Eustache F, et al., editors. Langage et aphasie. Bruxelles: De Boeck Université; 1993. p. 13–39.
[51] Legroux CJ. Recherches sur les concrétions sanguines dites polypiformes, développées pendant la vie. impr. Didot; 1827, Thèse Paris n° 215.
[52] Sée M. Société médicale des Hôpitaux: discussion sur l'artérite, l'embolie par MM. Béhier, Legroux, Barth, Gubler, G Sée. Gaz Hebd Med Chirur 1857;4(35):601–4.
[53] de Valicourt L. Etude clinique sur les hémiplégies observées dans le cours des pleurésies. imp. A. Parent; 1875, Thèse Paris n° 399.
[54] Virchow R. Thrombose und Embolie. Gefässentzündung und septische Infektion. In: Gesammelte Abhandlungen zur wissenschaftlichen Medicin. Frankfurt am Main: Von Meidinger & Sohn; 1856.
[55] Gubler A. Des paralysies dans leurs rapports avec les maladies aigues, et spécialement des paralysies asthéniques, diffuses, des convalescents. Arch Gen Med 1860;Ve série 15:693–713.
[56] Hillairet J. Dictionnaire historique des rues de Paris. Paris: Editions de Minuit; 1964.
[57] http://www.pa risdescartes.fr/content/download/1353/6997/version/1/file/grandHall.swf.