

4

Development of the nosology and classification of epilepsy: 1909–2009

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Considering the fact that in many minds to this day epilepsy is equated with generalised tonic–clonic seizures and with intractability, it is remarkable that even in the earliest preserved documents epilepsy is not seen as one homogeneous and necessarily untreatable disease.

In a Babylonian cuneiform text from the 7th or 8th century BC, different types of seizures are mentioned, explained by the ‘hand’ of different deities, and attributed different prognostic significance (Wilson & Reynolds 1990).

The idea of different gods being responsible for specific seizure types still reverberated in the first historical monograph on epilepsy, Hippocrates’ *On the Sacred Disease* of around 400 BC. He refuted supernatural explanations and referred the different symptoms to natural causes such as the properties of body fluids and the influences of winds and climate. He distinguished different courses in children, adults and the elderly, and knew that the course of epilepsy could often be benign; it only became intractable when it had prevailed too long.

In the Hellenistic period a triple concept developed, which with some modifications and changes of terms remained valid throughout the Middle Ages. In principle, epilepsy with origin in the brain was distinguished from cases where the brain was affected by some systemic disease, and those where, like with focal motor seizures or with epigastric auras, the seizures seemed to originate somewhere else and only secondarily reach the brain (Temkin 1971).

During these centuries, epilepsy was more or less synonymous with the generalised tonic–clonic or ‘grand mal’ seizure, the name by which it was known since the Middle Ages (Temkin 1971). The distinguishing traits were the known or presumed aetiology and the existence or absence of a focal motor onset. This changed in the 18th and 19th centuries when attention was increasingly

paid to other seizure types. Descriptions of absences were given by Poupart in 1705 (Temkin 1971), and Tissot in his monograph of 1770 reported a well-recognizable case of epilepsy starting at age 7 with absences with eyelid myocloni, which were 4 months later followed by convulsive seizures. The term ‘absence’, however, seems to have been one of the terms used by patients in the Paris hospitals and was introduced into medical literature in 1824 by Calmeil (Temkin 1971). Later were added focal motor or Jacksonian seizures (Bravais 1827; Jackson 1870), myoclonic seizures (Herpin 1867) and ‘psychic equivalents’ (see below). Status epilepticus, a latinisation of another patient term (*état de mal*) had long been known and individually described (Wolf *et al.* 2007) but was officially recognised by this term since Calmeil (1824).

It can be said that modern epileptology really started with Jackson when he became aware that more could be learned about the pathology of epilepsy from the study of ‘the simplest varieties of occasional spasm’ rather than the convulsions ‘usually called epileptic and sometimes cases of “genuine” or “idiopathic” epilepsy’ (Jackson 1870). He understood the anatomical implications of local convulsions and their ‘march’. Together with the neurosurgeon Horsley, he developed the concept of ‘focal’ epilepsy, and epilepsy surgery in the true sense started with Horsley’s operating on a patient where they had deduced the site of the underlying pathology from a precise analysis of the motor symptoms, comparing them with the patterns produced by stimulation of monkeys’ brains (Horsley 1886, case 2). Jackson’s delineations of ‘uncinate’ seizures (Jackson and Colman 1898) and of ‘trunk or lowest level fits’ (Jackson and Singer 1902) are other examples of his anatomical approach to the nosology of epilepsy.

Jackson was also the first author who was concerned with classification in epilepsy (Wolf 2003) although he never endeavoured to design a systematic classification. His concern was, rather, to get the fundamentals right before one started to build, and he clearly made the point that there were 'two ways of investigating diseases, and two kinds of classification corresponding thereto, the empirical and the scientific'. The object of the first was practical, i.e. the 'direct application of knowledge to utilitarian purposes', whereas the second, the 'classification properly so-called is rather for the better organisation of existing knowledge and for discovering the relation of new facts; its principles are methodical guides to further investigations. It is of great utilitarian value, but not directly.' Jackson's distinction is still highly relevant, and his comparison of the two approaches to the ways a gardener and a botanist would classify plants is famous to this day (Wolf 2003).

Towards the end of the 19th century, attempts appeared to bring systematic order into the field of epilepsy. Féré (1890), who wrote the first textbook on 'epilepsies' in the plural, distinguished primarily partial and generalised paroxysms and subdivided the latter into the following:

- 1 The complete attack
- 2 The incomplete attack
- 3 Abnormal attacks
- 4 Isolated symptoms

Binswanger (1899) used a similar classification which differed in one important item:

- 1 Epilepsia gravior
 - (a) The typical classic seizure
 - (b) The atypical attack
- 2 The rudimentary fit
- 3 Abortive attacks
- 4 Psychical epileptic equivalents

The last of these categories was a term which, according to Turner (1907), was first used by Hoffmann (1862). It related to a problem increasingly being discussed at the time: how to understand and where to place paroxysmal events that were neither generalised nor partial convulsions. These could occur in the same patients who had convulsive seizures but also in others where they were the sole manifestation, with identical phenotype. For Jackson, these represented another type of focal seizure for which he sought an anatomical substrate and related them to the uncinate gyrus. French and German neuropsychiatrists of the same period saw the matter differently.

They took a merely phenotypical approach and considered such seizures as psychic 'equivalents' of convulsive fits. However, this had consequences, because the borderlines between single psychomotor seizures (as they would be called later), clusters of such seizures, and more or less continuous twilight states of different duration are by no means sharp. This line of thought logically led to a concept of 'masked' epilepsy ('épilepsie larvée'; Morel 1860), the comparator always being epilepsy proper with generalised convulsive seizures.

These efforts at a conceptual re-organisation of epilepsy took place at a time when psychiatrists also struggled with the problem of finding an accurate nosological structure for the field of psychosis. The two parallel developments merged in the concept of epileptic insanity ('folie épileptique', Falret 1860; 'epileptisches Irresein', Samt 1875, 1876). The fundamental discovery was that one could have epilepsy without ever having suffered what was at the time recognized as an epileptic seizure. The effects were twofold: a group of important and frequent seizure types were rightly included into epilepsy, but a diagnosis of epilepsy could now also be applied to all sorts of extraordinary behaviour provided it occurred, at least initially, episodically or in a fluctuating manner.

A probable case in point is Vincent van Gogh. In 1889, psychiatrist Théophile Peyron of St Rémy-de-Provence diagnosed epilepsy in van Gogh, although he had never had a documented epileptic seizure.

Nosology of epilepsy in 1909

The discussion of psychic equivalents, masked and larval epilepsy by French and German psychiatrists had brought epilepsy into the contemporary conceptual discussion of psychiatric illness. Many of these psychiatrists worked in institutions and asylums for chronically ill people, and the epilepsy patients they saw there frequently developed psychoses as complications of severe seizure disorders, which were treated with occasionally heavy doses of bromide. Some authors even considered epilepsy primarily as a psychosis, and indeed the literature of the first decade of the 20th century is rich in publications on psychosis with epilepsy (Wolf 1976). In 1909, the year of the founding of the ILAE in Budapest, an important paper on epileptic psychoses and their treatment was published by German psychiatrist Ernst Siemerling (1909).

In Budapest, there was a special interest in the relations of epilepsy and schizophrenia or schizophrenia-like conditions. Thus, 2 of the 46 people who assisted with the foundation of the ILAE on 30 August 1909, Drs István (latinized Stefan) Hollós and Lajos Hajós, had at a society meeting the year before, together with Drs Jakob Salgó, Kálmán Pándy and Artúr von Sarbó, controversially discussed possible relations of epilepsy and paranoia (Hollós 1908), following the publication in 1907 by Hollós of four patients with this combination in the journal *Elme-és-Idegkörtan (Mind and Neuropathology)*. Hollós worked at the distinguished National Psychiatric and Neurological Institute in Budapest, and from 1913 onwards was one of the leading figures of Hungarian psychoanalysis.

The 1908 society minutes give early testimony of an interest in the combination of paranoid psychosis and epilepsy in Budapest, particularly at the institute where in the 1930s Nyírö and Jablonsky would observe that epilepsy remitted 16 times more frequently if the patients developed schizophrenic symptoms, and a similar 'biological antagonism' could be seen when schizophrenic patients had seizures. In consequence, László (alias Ladislás) von Meduna in 1934 at the institute would start to treat schizophrenia by pharmacologically induced seizures (Wolf and Trimble 1985).

Even though at the time psychiatry was particularly dominant, it did not exclude other views. In the years before and around the creation of the League, several authoritative textbooks appeared that more broadly reflected the nosological thinking of the time. William Gowers (1845–1915) had supplemented his 1881 work *Epilepsy and Other Chronic Convulsive Diseases* with *The Border-Land of Epilepsy* (1907). In 1907 William Aldren Turner (1864–1945) published *Epilepsy: A Study of the Idiopathic Disease* and Otto Binswanger's textbook *Die Epilepsie*, which was first published in 1899 and reflected the German psychiatric influence, appeared in 1913 in a second revised edition.

All these books use the term 'epilepsy' in the singular. For Gowers, epilepsy was essentially one disease, which he discussed with reference to aetiology (differentiating 'predisposing causes', including heredity, from 'exciting causes') and seizure types. These he described in some detail. Epilepsy following hemiplegia, hysteroid attacks and hystero-epilepsy appear as separate entities. Whereas Gowers did not employ the term 'epileptic equivalent', Turner, who was 19 years younger, fully adopted it. His

views were much closer to continental psychiatric concepts, and for him, epilepsy was not just a seizure disorder but typically comprised both a 'convulsive factor' and a 'psychical factor'. Although his book is about idiopathic epilepsy, he neither explicitly defined the term nor opposed it to others, probably under the influence of Reynolds, who 'employed the word "epilepsy" to denote only those cases in which no other disease was discoverable. The disease described in this Volume is, strictly speaking, idiopathic epilepsy; and I have here nothing to do with so-called symptomatic or sympathetic epilepsy' (Reynolds 1861). Turner cites Binswanger's 1899 classification of 'the clinical manifestations of the disease', which he elaborates as follows:

1 Minor epilepsy

- *Incomplete attacks*: aura without loss of consciousness
- *Complete attacks*: aura followed by some degree of impairment of consciousness, without obvious convulsion, but sometimes accompanied by a fall

2 Major epilepsy

- *Incomplete attacks*: refers to convulsive seizures where either the tonic or the clonic stage are slight
- *Complete attacks*: 'loss of consciousness with muscular spasm and convulsion of a tonic and clonic nature, followed by a characteristic after-stage of stupor. These attacks may, or may not, be preceded by an aura or warning'

3 Psychical epilepsy. Seizures 'in which the spasmodic element is slight and transitory, or is entirely absent, but in which the outstanding feature is revealed in automatic or semipurposive movements, consciousness being obliterated'

This basic structure was then further subdivided out into six 'categories', each of which presented three phases or degrees of seizure: (i) the aura, (ii) the incomplete fit and (iii) the complete fit. He quotes and confirms the 'law of identity' which had been proposed by Herpin (1867). It states that incomplete attacks which occur in the intervals between the major attacks are the complete seizures reduced to their initial symptoms, and that incomplete attacks, however diversified they may be, are always or nearly always similar in the same subject. Turner also points out, with explicit reference to Hughlings Jackson, that the initial symptoms of a seizure are those that point to the anatomical site of seizure onset. Therefore, the auras are the feature that determines his categories. These include the following:

- 1 Fits with warnings referred to the limbs
- 2 Fits with visceral warning
- 3 Fits with a warning of head sensations
- 4 Fits commencing with psychical warning
- 5 Fits with warnings referred to the organs of special sense
- 6 Fits without warning

The first category includes what we call bilateral myoclonic seizures: “shakes”, “jumps” or “starts” in the limbs, preparatory to the onset of the seizure, but these are more probably instances of “petit mal”, or minor seizures, rather than true warnings’.

In the text that follows, Turner also introduced en passant the term ‘psychomotor seizure’, without defining it but much in accord with his definition of psychical epilepsy. Well read in the continental literature and trying to amalgamate the best views of his masters at Queen Square, Gowers and Jackson, with the best of the German and French alienists, he devoted an entire one of the 12 chapters constituting his book to ‘the mental states found in epilepsy’, where he went into much detail about psychical epileptic equivalents. These he found very complex, difficult to delineate and of great consequence for the nosological concepts of epilepsy. Their discussion had widened the horizon of the epileptic phenomena. Did convulsions no longer matter in the diagnosis of epilepsy? Was periodicity the phenomenon on which the diagnosis of epilepsy should be based? Yet periodicity was not pathognomonic of epilepsy; all psychopathies presented irregular fluctuations in their clinical appearances. One was on safe ground when the supposed epileptic equivalents were associated in the same person with classic seizures; when there was uniformity in the appearance of recurring attacks; and when there was a definite relation of the symptoms to existing epileptic seizures, the equivalents occasionally occurring independently. Such clear conditions did not always exist, however, among other reasons because the equivalent could really be a post-paroxysmal psychosis following an attack ‘so slight, or so transitory, as to pass unobserved’. At the end, Turner defines ‘as *“psychical epileptic equivalents” the mental phenomena of the pre-and post-convulsive states, when they occur without convulsion or spasm* [italics Turner’s]’. This is followed by a classification of psychical epileptic equivalents:

- 1 Psychical epilepsy, consisting of two varieties:
 - (a) Short psychical attacks, or true psychical epilepsy
 - (b) Prolonged attacks, or epileptic ambulatory automatism

- 2 Epileptic mania, including the impulsions
- 3 Dream states
- 4 Temporary delusional states
- 5 Catatonic stuporous conditions
- 6 Cephalic and ‘aura’ sensations
- 7 Miscellaneous phenomena

The ‘chief epileptic impulsions’ are suicide, homicide and pyromania, but there are others, some of a bizarre and indecent type, such as theft, gluttony and exhibition. The dream states are paroxysmal states which can be found in all psychopathic subjects, and must not be confused with the dreamy states described by Jackson.

The dawn of epilepsy syndromes

The first syndromatic views now also began to take shape. Gowers (1881) drew attention to relations of seizures to the sleep–wake cycle. Twenty-one per cent of his 840 cases had seizures only or almost only during night sleep, 43% only or almost only by day. In 1% the seizures occurred only while going to sleep, and in 5% in the early morning (0.5% on waking up out of sleep). Gowers corroborated this earliest indication of epilepsy with grand mal on awakening in 1907, when he stated that ‘the state of awakening is one in which epileptic attacks are prone to occur in some subjects, and then are peculiarly difficult to influence’. Epilepsy following hemiplegia is the only symptomatic entity for which in 1881 he supplied his own description.

Turner (1907) grouped ‘the various ways in which epilepsy manifests itself clinically’ according to three aspects: seizure types, seizure frequency and the time of their occurrence. The seizure types were either all major (58.2%), all minor (3.8%) or a combination of both (38.2%). With respect to seizure frequency, three types stood out: serial epilepsy, status epilepticus and a type of epilepsy characterised by only a few fits. The time of occurrence referred either to the circadian distribution of nocturnal versus diurnal seizures, or to the age where senile epilepsy was separated out.

An early syndromatological controversy

One quite separate but interesting nosological discussion which had been started by the Mannheim neurologist Max Friedmann in 1906 concerned the place of ‘peculiar brief fits, especially in young people and children, which are similar to the petit mal of epileptics but neither symptomatically completely alike nor usually aetiologically

connected with epilepsy'. Here we have the first detailed and controversial exploration of one of the syndromes which are still recognised today. Friedmann identified these fits as absences, and asked whether they might be examples of larval epilepsy. He reports 15 from his own practice, 11 of which had reached adulthood. He gives beautifully detailed descriptions of typical childhood absences with retroversive movements of the head, occurring many times a day. These patients did not respond to bromide, but their prognosis was excellent as only one of 15 developed convulsive seizures. For this reason, Friedmann considered that these were not typically instances of epilepsy but, rather, belonged to the field of narcolepsy, a recently described entity which was still being debated.

His view was supported by several authors, not all of whom, however, agreed that what he was seeing was narcolepsy. Friedmann's finding was opposed by others, for example Gerard Christiaan Bolten (1916) of The Hague, who wrote a polemical paper presenting 14 own cases with different diagnoses. These included two with hysteria, whose common feature was minor fits that were very brief and very frequent and remained the only symptom at least for a considerable time. Mental deterioration was not always excluded. For Bolten, these cases represented an inhomogeneous group, no morbus sui generis, but 'nothing but the rudimentary form of the hysterical seizure, the seizure of cerebral epilepsy [his term for symptomatic epilepsy] and the seizure of genuine epilepsy'. In his descriptions we recognise cases of various types of both absences and focal seizures, and one each of juvenile myoclonic epilepsy and progressive myoclonus epilepsy.

Sauer (1916) of Greifswald disagreed a few months later in the same journal. The seizures of one of his eight patients also were psychogenic, but they differed from the others for whom he now proposed the term pyknolepsy, which endured. It was derived from the Greek πυκνός meaning 'dense' or 'frequent, heaped-up, closely packed, aggregated' (Adie 1924). His series seems to include two cases of frontal lobe epilepsy and one of myoclonic-astatic epilepsy, and he argued that the limits of pyknolepsy should not be drawn as narrowly as Friedmann had proposed. Pyknolepsy was a unique entity, different from both epilepsy and narcolepsy, but reliable differentiation from epilepsy was a major difficulty the individual cases. In a presentation to the section of neurology of the Royal Society of Medicine in London

on 8 November 1923, William John Adie reviewed 'numerous articles in foreign journals ... and the latest editions of the standard textbooks on nervous diseases' of which, however, he only quotes three (Friedmann, Heilbronner and Stieb). His detailed descriptions, probably based on his own cases, are not included in the printed report (Adie 1924), but he gives a precise definition of pyknolepsy (he advocates the use of the term) as 'a disease with an explosive onset between the ages of 4 and 12 years, of frequent short, very slight, monotonous minor epileptiform seizures of uniform severity, which recur almost daily for weeks, months or years, are uninfluenced by anti-epileptic remedies, do not impede normal mental and psychical development, and ultimately cease spontaneously never to return. At most the eyeballs may roll upwards, the lids may flicker and the arms may be raised by a feeble tonic spasm. Clonic movements, however slight, obvious vasomotor disturbances, palpitations, and lassitude or confusion after the attacks, are equivocal symptoms strongly suggestive of oncoming grave epilepsy, and for the present they should be considered as foreign to the more favourable disease'.

A recent paper by Valentin *et al.* (2007) came to quite similar conclusions, so we have perhaps made only modest progress since Adie. According to him, the favourable cases could not be immediately distinguished from ordinary petit mal. A certain period of observation was necessary prior to diagnosis. He was not greatly concerned with the question as to whether pyknolepsy was a disease sui generis. He found it most likely that it was 'a form of epilepsy in children which is distinguishable by its clinical features and in which the prognosis is always good'. The question of its nosological place was definitely settled by Lennox (1945), who found in the EEGs of patients with pyknolepsy spike and wave patterns that did not differ from absences in established epilepsy.

To sum up, at the time of the founding of the ILAE, unitarian views of epilepsy prevailed which, by the same token, sometimes required the exclusion of symptomatic cases as there was a growing awareness of a multitude of both aetiologies and seizure types. Moreover, for the first time, the plural form of the term had been used as the title of a textbook (Féré 1890). The pathogenesis of epilepsy was considered multifactorial, with both hereditary predisposition and manifestation factors.

Neurologists who treated patients living in the community, and neurosurgeons who operated on selected

patients, saw epilepsy primarily as a seizure disorder, whereas psychiatrists and those who treated patients living in asylums and institutions were inclined to view it as a more comprehensive organic brain disease where seizures even could appear as a mere epiphenomenon.

Developments after 1909

It may very well be that, had the ILAE been allowed to continue its work uninterrupted beyond 1914, it would already have attempted to develop an international consensus on these matters. But this is not what happened, and many different nosological concepts and schools with different terminologies and classifications appeared in the following decades.

In Germany, two divergent streams can be described. Neurologists such as Otfrid Foerster (1926) and neurosurgeons such as Fedor Krause (1911, 1931/32) developed great expertise in symptomatic focal, mostly neocortical epilepsies that could be surgically treated. In parallel, German-speaking neuropsychiatry adopted a concept of ‘genuine’ epilepsy, which resisted the influence of Jacksonian thinking in that it included auras and personality changes as primary symptoms. ‘Genuine’ was largely considered as synonymous with hereditary epilepsy, and this became highly consequential when, under the Nazi rule, sterilisation was enforced by law on patients with ‘hereditary falling sickness’. This nosological misconception ‘added to the infamy of forced sterilisation the grotesquerie that to a large extent even the wrong people were sterilised’ (Wolf 1989). Nosology is not always an ivory tower concept.

After the Second World War, German epileptology had a new start which, under the influence of British neurology, did away with the old psychiatric views that had both failed to protect and even exposed patients to Nazi transgressions. The view that personality changes, including slowness, stickiness and pedantry, bigotry and hypersocial behaviour (Samt 1876), were an integral part of the clinical picture of ‘genuine’ epilepsy to the extent that their absence would cast doubt on the diagnosis (Stauder 1938) was now criticised and replaced by a different view which tried to distinguish the influences of brain damage (either pre-existent or caused by trauma or status epilepticus), high doses of phenobarbital, as well as psychosocial factors such as reaction to stigma or, in

some asylums where these views had originated, adaptation of institutionalised patients to the expectations of religious leadership (Janz 1969).

In Heidelberg, where no EEG was available until the mid-1950s, neurologists Dieter Janz and Walter Christian, and paediatricians Ansgar Matthes and Rolf Kruse, started a series of analyses of epilepsies of childhood and adulthood which paid attention to diverse biological features such as age-dependence, relation of seizures to biorhythmicity, patterns of co-occurrence of various seizure types and motor patterns. Their most important contributions were the description of juvenile myoclonic epilepsy (Janz and Christian 1957) and the delineation of epilepsy with grand mal on awakening (Janz 1953), which both later became part of the concept of idiopathic generalised epilepsy. At the same time, Hermann Doose in Kiel described the syndrome of myoclonic-astatic epilepsy (Doose *et al.* 1970).

The textbook on epilepsy by the Dutch neurologist L.J.J. Muskens, one of the co-founders of the League and of *Epilepsia* (Muskens 1926; see Chapters 1 and 7) was too much focused on personal theories about the central role of myoclonus in epilepsy to be broadly influential.

The developments in France were recently described in detail by Beaumanoir and Roger (2007) who themselves have made significant contributions. In French epileptology, with the exception of Pagniez (1929), the view of epilepsies in the plural had taken hold, as is documented by the textbooks of Marchand and de Ajuriaguerra (1948) and Roger *et al.* (1950). More importantly, it was here that the effect of the new technology of the electroencephalography on the nosology of the epilepsies was most rapidly felt.

The influence of electroencephalography

The most profound influence on the nosology of epilepsy in the 20th century was Hans Berger’s introduction of EEG into the study of the disease in 1924. Although he published 23 papers on the subject in quick succession, the development was initially slow to be recognised in Germany, and in fact was first used and further refined in North America, where it immediately gave rise to new considerations on nosology and classification. In 1935, William G. Lennox’s presentation of EEGs from patients at the 2nd International Congress of Neurology in London caused a sensation. (Berger’s fate was tragic. His opposition to the Nazis ended his career in 1938. He committed

suicide in 1941.) Frederic A. Gibbs *et al.* published their first paper on the EEG in epilepsy in 1937, and proposed to consider the disease as a cerebral dysrhythmia. They found that the EEG patterns ‘classified into three main groups which agree with the three main clinical types of seizures: (1) Grand mal, having a fast rhythm, up to 25–30/sec and appearing as sharp spikes. (2) Psychomotor attacks (psychic variants), accompanied by slow (3–7/sec) high voltage, square topped waves. (3) Petit mal, having an alternating fast and slow rhythm’. On this basis, Lennox (1945) a few years later developed the nosological concept of the petit mal triad: absences, bilateral myoclonus, and akinetic or astatic seizures.

The surgical orientation of the Montreal school led to a different view. To Jasper and Kershman (1941) the form of the dysrhythmia seemed to be much less important than the location and distribution of the abnormal rhythms and their correlation with seizure type. They distinguished between focal cortical, projected subcortical (e.g. spikes and slow waves) and diffuse dysrhythmias.

The French school particularly welcomed and developed the new method, starting with papers by Baudoin *et al.* (1938) and Pagniez (1937). In Marseilles, the group of Henri Gastaut, Joseph Roger, Anne Beaumanoir, Charlotte Dravet and Michelle Bureau as the permanent nucleus, with a series of collaborators from France, Italy (e.g. Carlo Tassinari and Bernardo dalla Bernardina) and various other countries over the next decades, published numerous reports on syndromatic entities which give evidence of an outstanding culture of acuity and gestalt perception which usually comprised a clinical picture and special EEG traits.

The international classifications

It was Gastaut who took the initiative to create an international classification because ‘current classifications of epileptic seizures vary considerably, and the need for a standardised and uniform system of grouping is very apparent’ (Gastaut *et al.* 1964). For this purpose, 120 members of several European branches of the ILAE met in Marseilles on 1–2 April 1964. A draft was produced and submitted to a commission on terminology ‘consisting of representatives of the American and European Branches of the ILAE and of representatives of the World Federation of Neurology and of the International Federation

of Societies for Electroencephalography and Clinical Neurophysiology (IFSECN)’. The speed was remarkable given that the new commission already met again on 11–13 May 1964 at Meer en Bosch in Heemstede, The Netherlands, and still in the same year managed to publish in *Epilepsia* a proposal for an International Classification of Epileptic Seizures (Gastaut *et al.* 1964). The commission recognised ‘that all attempts at classification of seizures are hampered by our limited knowledge of the underlying pathological processes within the brain and that any classification must of necessity be a tentative one and will be subject to change with every advance in scientific understanding of epilepsy’. This proposal considered the categories clinical seizure type, electroencephalographic expression (both ictal and interictal), anatomical substrate, aetiology and age, and was quite detailed (Table 1). Although numerous and in some cases significant changes were later made, most of this draft of 1964 remained, establishing the fundamental structure for an international seizure classification.

Members of the League were invited to send ‘comments and proposals for modification to [Gastaut], so that they may be studied prior to the presentation’ that took place at the quadrennial meeting of the ILAE in Vienna, on 5 September 1965. In a process later described by Gastaut (1970), then secretary-general of the ILAE, the scheme was further discussed and presented in a revised form to the 11th meeting of the League in New York on 27 September 1969 and then published. However, disagreement persisted on several points, and the classification seems never to have been formally approved (Gastaut 1970). However, it was widely adopted, as there was a definite need for it. Subsequent ILAE commissions continued to ‘update, amend and improve the classification in the light of the capability afforded by the newer techniques to study seizures’ (Commission 1981). This refers to ‘video display of epileptic seizures on magnetic tape, the simultaneous recording of the electroencephalogram using hard-wired recording techniques and radiotelemetry with split screen display and instant replay capability’.

This approach was revolutionary because, for the first time, it introduced objective methods of analysing seizures for classification instead of relying on the judgement of experts based on their ability to distil abstract ideal types from the numerous seizures they observed. A series of workshops were held by the commission where consensus

138 International League Against Epilepsy 1909–2009 A Centenary History

Table 1 Gastaut's proposed International Classification of Epileptic Seizures (1964).

1 Partial seizures

A With elementary symptomatology

- 1 With motor symptoms
 - (i) focal motor (without march)
 - (ii) Jacksonian
 - (iii) adersive
 - (iv) postural
 - (v) somatic inhibitory
 - (vi) phonatory (vocalisation and speech arrest)
- 2 With special sensory or somatosensory symptoms
 - (i) somato-sensory
 - (ii) visual
 - (iii) auditory
 - (iv) olfactory
 - (v) gustatory
 - (vi) vertiginous
- 3 With autonomic symptoms
- 4 Compound forms

B With complex symptomatology (which may sometimes begin with elementary symptomatology)

- 1 With impaired consciousness alone
- 2 With intellectual symptomatology
 - (i) with dysmnestic disturbances (including amnesia, déjà vu, déjà vécu)
 - (ii) with ideational disturbances (including 'forced thinking')
- 3 With affective symptomatology
- 4 With psychosensory symptomatology (illusions, hallucinations)
- 5 With psychomotor symptomatology (automatisms)
- 6 Compound forms

C *Secondarily generalised* (all forms of partial seizures, with elementary or elaborated symptomatology, can develop into generalised seizures, sometimes so rapidly that the focal features may be unobservable. These generalised seizures may be symmetrical or asymmetrical, tonic or clonic, but most often tonic-clonic in type). [It was explained that complex in distinction from elementary implied organised high-level cerebral activity, whereas compound implied a joining together of elementary or complex symptoms.]

2 Generalised seizures

A Non-convulsive seizures

- 1 With impairment of consciousness only
 - (a) Brief duration (beginning and ending abruptly)
 - (i) typical absence
 - (ii) atypical absence
 - (b) Long duration (absence status)
- 2 With other phenomena associated with impairment of consciousness: absences, typical or atypical, and absence status can occur
 - (i) with mild clonic components (myoclonic absences)
 - (ii) with increase of postural tone, symmetrical or asymmetrical (absences with retropulsion or gyration)
 - (iii) with diminution or abolition of postural tone ('drop attacks' or atonic seizures of longer duration)
 - (iv) with automatisms
 - (v) with autonomic phenomena (some forms of abdominal seizures, absences associated with sphincter incontinence etc.)
 - (vi) as mixed forms

B Convulsive seizures

- 1 Myoclonic jerks
 - (i) generalised (including the shortest 'infantile spasms')
 - (ii) fragmentary
- 2 Clonic seizures
- 3 Tonic seizures (including the longest 'infantile spasms')
- 4 Tonic-clonic seizures

Continued

Table 1 (continued) Gastaut's proposed International Classification of Epileptic Seizures (1964).**3 Unilateral or predominantly unilateral seizures in children**

Characterised by clonic, tonic or tonic-clonic convulsions, with or without an impairment of consciousness, expressed only or predominantly in one side. Such seizures sometimes shift from one side to the other but usually do not become symmetrical

4 Erratic seizures in new-born

With variable tonic and/or clonic convulsions, generally unilateral, sometimes alternating or generalised

5 Unclassified epileptic seizures

Includes all seizures which cannot be classified because of inadequate or incomplete data

Addendum

Epileptic seizures have just been considered in the light of clinical, electroencephalographic, anatomical and aetiological factors. They may also be classified according to their frequency.

- 1 Isolated seizures [*exemplified by febrile and eclamptic convulsions*]. While these are epileptic phenomena, in every day usage they are not referred to as forms of epilepsy
- 2 Repeated seizures occur under a variety of circumstances:
 - (i) as fortuitous attacks, coming unexpectedly and without any apparent provocation;
 - (ii) as cyclic attacks, at more or less regular intervals (e.g. in relation to the menstrual cycle or the sleep-waking cycle)
 - (iii) as attacks provoked by: (a) non-sensory factors (fatigue, alcohol, emotion, etc.); or (b) sensory factors, sometimes referred to as 'reflex seizures'
- 3 Prolonged or repetitive seizures (status epilepticus)

was reached on the seizures presented. The revised seizure classification based on this procedure was sent to the chapters for comments, and finally published as 'a compromise which represents a synthesis of the efforts of many persons examining hundreds of seizures over many years. This compilation of knowledge has been brought in line with the state-of-the-art technology without extrapolating to what cannot be observed, but cognizant of the evanescence of any living semantic endeavor which must remain subject to continual revision' (Commission 1981). It was accepted by the General Assembly of the ILAE and remains valid at the time of writing.

The abstention from 'extrapolating' refers above all to possible conclusions regarding the anatomic substrates and aetiologies which cannot be based on direct observation. The 1981 classification is, thus, a fundamentally semiological classification. A peculiar feature deriving from the applied method of analysis is that it does not look at a seizure as a complete gestalt but rather as a sequence of events that evolve in time.

The classification of syndromes

Once the discussion on seizure classification seemed to have reached a preliminary endpoint in 1969, the commission felt that a second step needed to be taken, namely to supplement the seizure classification with a classification of epilepsies. A draft written by Gastaut was

submitted to the commission, discussed at the occasion of the international congress in New York on 27 September 1969, presented to the ILAE General Assembly and published (Merlis 1970) with the intention of starting a discussion process similar to that for seizure classification. However, owing to the complexities of the first classification, the draft of the second (which fundamentally represented a generalised versus partial dichotomy built upon seizure types, so much remained to be done) was left lying until 1981, when a new Commission on Classification and Terminology with Peter Wolf as chair was asked to take up the thread. This commission (see Chapter 2) was well-composed: the major schools were represented, which forced them to reconcile their often divergent views. They rapidly agreed on a general framework consisting of a double dichotomy:

- | | |
|------------------------------|---------------------------------------|
| • Idiopathic
generalised | • idiopathic
localisation-related |
| • Symptomatic
generalised | • symptomatic
localisation-related |

It was recognised that some cases could not definitely be allocated to one side of the dichotomy or the other because of either insufficient or conflicting evidence. There also needed to be a group of special syndromes such as febrile convulsions.

This classification uses an additional dichotomy to that of seizures, distinguishing idiopathic from symptomatic

cases. In the 1970 draft, the terms ‘primary’ (for cases where epilepsy is the primary or only disease) and ‘secondary’ (where it is due to an underlying brain pathology) had been proposed, with some hesitation and an invitation to propose alternatives. This terminology had produced much confusion. In particular, ‘secondary generalised epilepsy’ was broadly misunderstood as signifying cases with secondarily generalised tonic–clonic seizures, that is generalised tonic–clonic seizures of focal onset. For patients with only this seizure type, the term ‘partial’ seemed also inappropriate and potentially confusing. But the term ‘focal’, which did apply well to these seizures, did not fit the idiopathic childhood epilepsies with partial or focal seizures because they had no demonstrable structural or functional focus and could arise alternately from corresponding localisations of either hemisphere. Accordingly, the commission introduced a neologism, ‘localisation-related’, as a preliminary term until the pathophysiology of these epilepsies was better understood, and usable for all syndromes characterised by partial or focal seizure types.

An important event in the development of the classification was a workshop organised by Joseph Roger in Marseilles on 7–10 July 1983, where the commission met with the international clinicians who had proposed syndromes, to have the evidence presented and exposed to critical peer review. At the end, the commission selected those syndromes that seemed to be sufficiently established to be included in the above classification framework. Review papers on these and other syndromes in development were published as a volume in French and in English (Roger *et al.* 1985), which became popularly known as the ‘Guide bleu’ of epileptology and now exists in its fourth revised edition (Roger *et al.* 2005).

The international classification of epilepsies and epileptic syndromes was presented to the General Assembly of the ILAE in Hamburg (Commission 1985) and accepted with some revisions in New Delhi (Commission 1989). The most important change was the addition of a class of cryptogenic epilepsies for cases where no proof existed of their belonging to either the idiopathic or the symptomatic category. This would mostly apply if a symptomatic aetiology was suspected but could not be proved.

Recent developments

With the seizure classification of 1981 based upon expert consensus about objective data, and the syndrome classification of 1989 based on critical reviews of the proposed

entities which were extensively discussed by a group of experts from different schools, the ILAE had succeeded in putting into a taxonomic framework what was considered to be the well-established knowledge of the time.

But the League could not rest on its laurels. As the introduction of the 1981 seizure classification clearly spelled out, it was merely a ‘skeleton’ to be ‘fleshed out and the nuances elaborated’. A mechanism was needed for constantly integrating new knowledge as it was acquired, reviewing and accepting newly described syndromes and so on. Also, the classifications were fundamentally taxonomies which provided little guidance on how to apply them to the clinical situation. They needed to be supplemented by a diagnostic manual.

None of these critical steps was reached, however, a lack that in the 1990s resulted in increasing criticism, especially of the seizure classification and by groups active in epilepsy surgery who were asking for much more detail including, if possible, anatomical conclusions (Lüders *et al.* 1993). The Cleveland Clinic group proposed their own system to replace the international seizure classification (Lüders *et al.* 1998). At that time, Pete Engel, ILAE president since 1997, had appointed a task force chaired by himself which expected to propose a revised classification to the General Assembly in 1999. The problems to be solved proved too intricate, however, and it was not until 2001 that the task force proposed to the General Assembly in Buenos Aires not a new taxonomy but a diagnostic manual or scheme (Engel 2001) that was accepted as a discussion document.

The work on these matters has since continued and has now come to a very interesting point where the dual dichotomy is indeed in question in the light of new findings on genetics, advanced functional and structural imaging techniques, and more sophisticated neurophysiological methods. The term ‘generalised’ is likely to disappear as we begin to better understand the functional anatomic networks and circuits involved in the ictogenesis of these as well as the idiopathic localisation-related epilepsies. A new concept of ‘system epilepsies’ seems to be about to replace the traditional dichotomy, as was discussed in great detail in the spring of 2008 in Monreale, Sicily, by a group of interested epileptologists, including most of the members of the present Commission on Classification and Terminology chaired by Anne Berg. The report of this meeting (Capovilla *et al.* 2009) is an excellent and comprehensive summary of where the ongoing nosological discussion stands 100 years after the foundation of the ILAE.

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