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Chapter

Definition, Classification, and Burden of Epilepsy

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Abstract

Epilepsy is one of the most common neurological diseases in the world, and is characterized by recurrent unprovoked seizures (fits) that can occur at all ages. The causes of epilepsy are multiple, ranging from perinatal problems, traumatic brain insults, metabolic abnormalities, to infections of the central nervous system; sometimes, the causes are not known. Consensual international norms have been established for the proper diagnosis and management of epilepsy, including specificities for vulnerable populations such as children and pregnant women. Specific emphasis must be laid on low and middle income countries, where about 80% of all persons with epilepsy reside. In such resource-limited settings, epilepsy patients are often confronted with sub-optimal care, reduced access to treatment, and frequent epilepsy complications. Early epilepsy diagnosis and proper anti-epileptic treatment usually result in satisfactory seizure control, and enable persons with epilepsy to lead a normal life. Besides the usual medications, psychosocial support and stigma reducing interventions are crucial to improve the quality of life of affected persons and their families.

Keywords: epilepsy, seizure, epidemiology, etiology, management

1. Introduction

Epilepsy is a chronic disease of the brain estimated to affect 50 million people worldwide according to World Health Organization (WHO) [1]. It is characterized by repetitive, unprovoked epileptic seizures which vary widely in their clinical presentations. Although a meticulous patient history complemented by sound clinical/paraclinical investigations often unveil the underlying cause of epilepsy, the exact etiology remains unknown in about half of cases [2]. Proper diagnosis and treatment of epilepsy are paramount to achieve seizure control and ensure an optimal quality of life for affected individuals.

1.1 Definition of epilepsy

In 2005, the International League Against Epilepsy (ILAE) defined epilepsy as "a disorder of the brain characterized by an enduring predisposition to generate epileptic seizures, and by the neurobiologic, cognitive, psychological, and social consequences of this condition" [3]. An epileptic seizure, on the other hand, refers to "a transient occurrence of signs and/or symptoms due to abnormal excessive or synchronous neuronal activity in the brain" [3]. While these definitions remain very conceptual, they are difficult to apply in a real-life clinical setting.

Therefore, a Task Force was commissioned to formulate an operational definition of epilepsy; the definition of epilepsy was thus broadened to accommodate three practical circumstances (**Box 1**) [4].

Epilepsy is a disease of the brain defined by any of the following conditions:

- At least two unprovoked (or reflex) seizures occurring >24 h apart
- One unprovoked (or reflex) seizure and a probability of further seizures similar to the general recurrence risk (at least 60%) after two unprovoked seizures, occurring over the next 10 years
- Diagnosis of an epilepsy syndrome

Epilepsy is considered to be resolved for individuals who had an age-dependent epilepsy syndrome but are now past the applicable age or those who have remained seizure-free for the last 10 years, with no seizure medicines for the last 5 years.

Box 1.
Operational (practical) clinical definition of epilepsy [4].

Emphasis must be laid on some points in this operational definition. Firstly, the seizures must be unprovoked, and not as a result of an acute, punctual event such as head trauma, substance abuse/withdrawal, metabolic imbalance, infection of the central nervous system or fever. As concerns the minimal risk of recurrence fixed at 60%, it is merely approximative of the likelihood of future seizure (mostly based on paraclinical findings on the electroencephalogram (EEG) or brain imaging [5]) and should not be interpreted as an absolute cut-off [4]. Another point to note is the minimal time difference of 24 hours between the seizures, but without a maximum time interval; in practice, the ILAE maintains the lifetime occurrence of two unprovoked seizures as a diagnostic criterion for epilepsy. Finally, epilepsy syndromes have been elaborately documented by the ILAE; each syndrome is characterized by specific electroclinical and/or genetic features [6].

1.2 Diagnosis of epilepsy

The diagnosis of epilepsy is essentially clinical. Based on the criteria listed in **Box 1**, the epilepsy diagnosis can be made if an individual fulfills the ILAE criteria. In a hospital setting, the following paraclinical workups can be performed to further investigate the epilepsy diagnosis: EEG, brain imaging (by scan or magnetic resonance), and blood tests (to investigate metabolic or genetic epilepsies).

In field research settings, the ILAE recommends epilepsy assessment using a door-to-door approach [7]. Several tools have been developed for epilepsy screening during epilepsy studies [8–11]; for studies conducted in the sub-Saharan setting in particular, the Institute of Neurological Epidemiology and Tropical Neurology of Limoges (France) developed a questionnaire with the support of the Pan-African Association of Neurological Sciences and the ILAE (Commission on Tropical Diseases, 1993–1997) [11]. This questionnaire was validated in Mauritania (sensitivity: 95.1%; specificity: 65.6%) and has since then been widely used for epilepsy surveys in Africa [11]. It has the advantages of being brief, usable by non-physicians, and diagnosing seizure types other than generalized tonic-clonic episodes (for instance, absences and focal seizures). To ensure accurate outcomes, it is important that a neurologist or physician trained in epilepsy confirms all suspected epilepsy cases clinically, following the ILAE diagnostic criteria.

1.3 Epidemiology and burden of epilepsy

Although epilepsy occurs in a ubiquitous manner, its burden is unevenly spread in different regions of the world depending on the local distribution of risk factors, access to treatment, and population demography. A recent meta-analysis found an overall lifetime prevalence of epilepsy of 7.60 per 1000 population (95% CI 6.17–9.38); this was higher in low and middle income countries (LMICs) (8.75 per 1000; 95% CI 7.23–10.59) than in high income countries (5.18 per 1000; 95% CI 3.75–7.15) [12]. A similar pattern was observed regarding epilepsy incidence: it was higher in LMICs compared to high-income countries, 139.0 per 100,000 person years (95% CI 69.4–278.2) vs. 48.9 per 100,000 person years (95% CI 39.0–61.1) [12].

These numbers clearly demonstrate that epilepsy poses a greater problem among populations living in LMICs compared to those in industrialized countries [2]. Indeed, nearly 80% of the global burden of epilepsy occurs in the people living in LMICs [1]. In sub-Saharan Africa specifically, a median epilepsy prevalence of 14.2 per 1000 (IQR 8·0–33·2) was documented, with over 90% of cases being younger than 20 years [13]. Annual epilepsy incidence was also high, reaching 81.7 per 100,000. Mortality was greatest in the 18–24 years age group, suggesting a relatively low life expectancy among persons with epilepsy (PWE) in Africa [13]. Suggested explanations for this pattern include the epilepsy risk factors that are often reported in resource-poor settings such as perinatal brain insults, traumatic head injury and infections of the central nervous system [13]. A variable genetic predisposition to manifest seizures in different populations may also explain the regional disparities observed in the occurrence of epilepsy worldwide, as people of different ethnic origins within a given population were found to have different incidence rates for epilepsy [14].

According to the 2016 Global Burden of Disease Collaborators, epilepsy accounted for >13 million Disability Adjusted Life Years (DALYs – a measure of the number of years of healthy life lost to epilepsy within a given population), and was responsible for 0.5% of the total disease burden in 2016 [15]. Again, important geographical differences were noted with epilepsy ranking among the top five neurological diseases in low-income regions. That study also found significant reductions in mortality and DALY among PWE between 1990 and 2016, reflecting some improvement in epilepsy healthcare and treatment.

2. Seizure/epilepsy classification and etiologies

International standards and norms have been adopted to classify seizures and epilepsies.

2.1 Classification of seizures

In 2017, the ILAE released the most recent guidelines for classifying seizures and epilepsies [5, 6, 16, 17]. Seizure classification begins with the mode of onset, whether focal or generalized [16]; the onset may also be unknown if the patient/caregiver does not recall the details of the initial seizure manifestations. Focal-onset seizures are further categorized into two depending on the state of consciousness during any part of the seizure: retained awareness versus impaired awareness (**Figure 1**) [16]. Irrespective of whether the onset is focal or generalized, seizures are grouped based on their physical manifestations as being motor (visible external movements) or non-motor (**Figure 1**). There is also a special group for focal

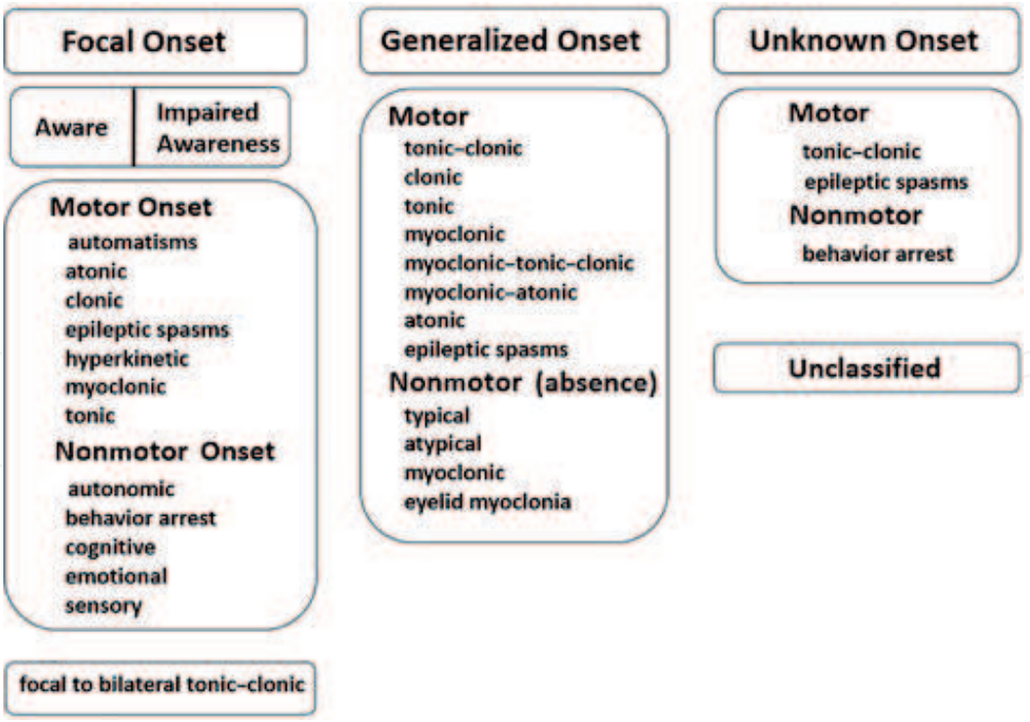

Figure 1.
ILAE 2017 classification of seizure types (extended version) [16] (used with permission).

onset seizures which evolve to generalized seizures, known as focal to bilateral tonic-clonic seizures [16]. Of note, absence seizures are considered as generalized non-motor seizures [16]. However, in case some seizure descriptions do not appropriately fit into any of these categories, they can be considered as "unclassified".

2.2 Classification of epilepsies

For epilepsies, the classification starts with the seizure type [6], and the certainty that the nature of the seizure(s) justifies the diagnosis of epilepsy [4]. Patients who do not meet criteria for epilepsy (for example, a single seizure or repeated provoked seizures) should be classified as to a seizure type, but classification should stop there [5]. Once the epilepsy diagnosis is confirmed, the epilepsy type can be deduced as focal, generalized, combined generalized & focal, or unknown (**Figure 2**) [6]. The epilepsy type is decided mainly on clinical grounds, and the diagnosis may be supported by EEG findings [6]. The final (facultative) level in epilepsy classification is the epilepsy syndrome diagnosis; an epilepsy syndrome refers to a cluster of features incorporating seizure types, EEG results, and brain imaging features that tend to occur together [6]. Each epilepsy syndrome often has specific features such as age at onset and remission (where applicable), seizure triggers, diurnal variation, and sometimes prognosis. Distinctive co-morbidities such as intellectual and psychiatric abnormalities may also be associated with specific epilepsy syndromes, as has been observed with the nodding syndrome [18]. Other common epilepsy syndromes include: Childhood Absence Epilepsy, Juvenile Absence Epilepsy, Juvenile Myoclonic Epilepsy, and Generalized Tonic-Clonic Seizures Alone; these are all forms of idiopathic generalized epilepsies [6]. Classification of epilepsy into syndromes often has etiologic, prognostic, and treatment implications [6].

A new feature in the 2017 epilepsy classification is that it integrates an etiology component as well as co-morbidities in epilepsy (**Figure 2**). Six etiological axes were enumerated by the ILAE task force: structural, genetic, infectious, metabolic,

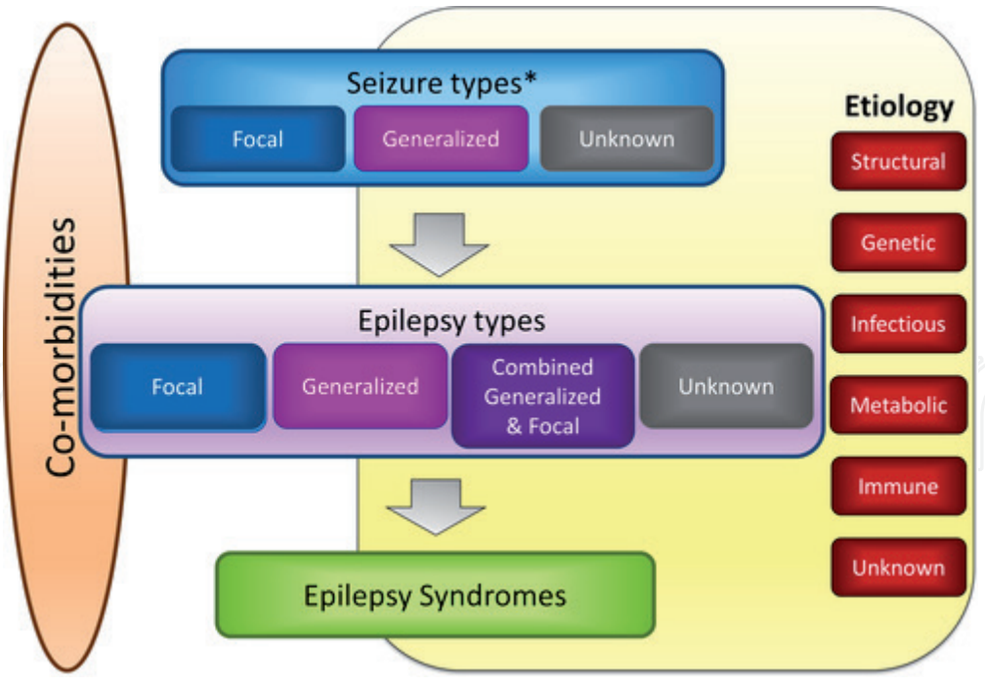

Figure 2.
ILAE framework for the classification of epilepsies [6] (used with permission).

immune, and unknown etiologies. Co-morbidities which should be considered on a case-by-case basis when diagnosing/classifying epilepsy include: intellectual decline, psychiatric and behavioral abnormalities, psychosocial problems, sleep disorders, and motor deficits [6].

2.3 Epilepsy etiologies

2.3.1 Structural etiologies

These are caused by structural brain abnormalities which have been shown to substantially increase the risk of developing epilepsy. These abnormalities are usually detectable by neuroimaging and in association with electroclinical assessments, lead to a reasonable inference that they are responsible for the enduring predisposition to unprovoked seizures [3, 6]. Structural etiologies could be primitive (for instance congenital malformations), or acquired (from a stroke, head trauma, infection, hypoxic-ischemic encephalopathy) [6].

2.3.2 Genetic etiologies

Epilepsy etiology is considered as genetic if there exists a specific disease-causing variant in a gene or copy number variant, believed to be the explanation for the observed epileptogenicity [5]. Of note, genetic mutations are not always inherited, as several epileptogenic de novo mutations have been identified [6]. The genetic alteration often causes a very heterogeneous phenotypic spectrum. A few genetic epilepsies identified to date include: the syndrome of Benign Familial Neonatal Epilepsy (KCNQ2 or KCNQ3 mutations) [19] and the Dravet syndrome (SCN1A mutations) [20].

2.3.3 Infectious etiologies

These are the most common preventable causes of epilepsy, particularly in sub-Saharan Africa [13, 21]. The concept of an infectious etiology is that the epilepsy

directly results from a known infection in which seizures are a core symptom [6]; it is the persistence of these seizures even after resolution of the acute infection that is referred to as epilepsy of infectious origin. Common examples of infectious etiologies include neurocysticercosis, tuberculosis, HIV, cerebral malaria, subacute sclerosing panencephalitis, cerebral toxoplasmosis, and congenital infections such as Zika virus and cytomegalovirus [6, 22]. A recent cohort study supports the addition of onchocerciasis to this list, as the more infected participants had an increased risk of developing epilepsy later in life [23]. These infections sometimes have a structural correlate to explain the seizure recurrence even after anti-infectious treatment; this results in a substantial overlap with the acquired structural causes of epilepsy [5].

2.3.4 Metabolic etiologies

In some cases, the core cause of the epilepsy results from a metabolic derangement. Clinical entities such as porphyria, uremia, aminoacidopathies, or pyridoxine-dependent seizures all fall within this category. These conditions may also be associated with a pre-existing genetic defect, although a few can be acquired such as cerebral folate deficiency [6].

2.3.5 Immune etiologies

There are a rising number of persons in whom the epilepsy is caused by an autoimmune condition, as evidenced by an autoimmune-mediated central nervous system inflammation [6]. Examples include anti-NMDA (N-methyl-D-aspartate) receptor encephalitis and anti-LGI1 encephalitis [24]. The anti-leimodin antibodies hypothesis for central nervous system damage would equally place Nodding syndrome in this category [25].

2.3.6 Unknown etiology

For many PWE, the exact etiology may not be known. In such cases, diagnosis and management are solely based on electroclinical findings [6]. Nevertheless in some settings, epidemiological observations may provide clues as to a possible epilepsy etiology within a given vicinity. For instance, a pooled analysis of 37 studies showed that the etiologic fraction of epilepsy was estimated to be 63.0% (95% CI: 61.4 ± 64.5) in persons exposed to cysticercosis [26]. Therefore, in cysticercosis-endemic settings, it would be reasonable to assume that a considerable number of epilepsy cases are due to neurological complications of *Taenia solium* infection even without laboratory confirmation. Similarly, in onchocerciasis-endemic villages of Cameroon, the contribution of infection with *O. volvulus* to epilepsy was very high (population-attributable fraction: 91.7%, 95% CI 56.7–98.4; p = 0.0021) [23]. Hence in communities with proven high ongoing transmission of *O. volvulus*, many epilepsies of "unknown" etiology could as well be caused by onchocerciasis.

3. Epilepsy management in specific settings

About four fifth of PWE currently reside in LMICs where epilepsy care is often sub-optimal, resulting in a 75% treatment gap (proportion of PWE needing treatment who do not receive the necessary anti-epileptic drugs) [1]. It is therefore important to discuss epilepsy in these contexts, and propose ways to improve PWE management in such settings. Another special population worth looking into is the

women of reproductive age suffering from epilepsy. The risk with these women is the teratogenic effects of anti-epileptic drugs, which renders their management before, during, and after pregnancy quite delicate.

3.1 Managing epilepsy in resource-limited settings

Improved management of PWE in resource-limited settings may be achieved by decentralizing epilepsy care. Approaches to diagnose and manage epilepsy and related complications can be simplified and taught to non-physicians, who will be in charge of running local epilepsy clinics under the supervision of physicians or specialists [27, 28]. Setting up a community-based epilepsy surveillance system will enable early diagnosis and treatment of PWE thereby preventing complications. To reduce the treatment gap, a regular supply of subsidized anti-epileptic drugs (AEDs) appropriate for different seizure types should be instituted. Daily intake of the adequate AEDs would eventually achieve seizure control in at least 70% of PWE [1]. The first-line AEDs that are routinely used in sub-Saharan Africa include phenobarbital, carbamazepine, phenytoin, and valproate [29]. Their indications and prescribed dosages as recommended by the WHO are detailed in **Table 1** [30]. AED treatment must be initiated as monotherapy with progressive dose increase based on the response to the treatment and seizure control. Phenobarbital, the most available and affordable AED (annual cost per PWE: 5 US dollars [29]), is used as first-line treatment for most seizure types but is not recommended for absences. It is usually initiated at 2–3 mg/kg/day and could be increased every 2–3 weeks by 15 mg if seizures continue, without going above the maximal recommended dose. When switching to another AED, phenobarbital should be tapered progressively (15 mg reduction every 2 weeks) while starting the newly prescribed AED as soon as the tapering begins. This approach minimizes the risk of rebound seizures upon stopping phenobarbital [31].

Besides the AEDs in **Table 1** which are commonly used in resource-limited settings, newer AEDs have been developed and are widely used in high-income countries; these include: gabapentin (GBP), topiramate (TPM), lamotrigine (LTG), levetiracetam (LEV), rufinamide (RFN), vigabatrin (VGB), oxcarbazepine (OXC), perampanel (PER), lacosamide (LCM) and eslicarbazepine acetate [36]. Although these are more expensive and less available in LMICs compared to the routine first-line AEDs, they are superior in achieving seizure control with relatively less side effects and fewer drug interactions.

Another essential component of epilepsy care in resource-limited settings is stigma reduction. In rural communities of Africa, PWE and their families are often stigmatized as a result of misconceptions regarding the origin and transmissibility of epilepsy [37]. Therefore, it is important that community awareness programs on epilepsy, as well as other interventions should be implemented to reduce stigma and facilitate the social rehabilitation of PWE [38].

3.2 Epilepsy in women of child-bearing age

In addition to seizures and related complications experienced by all PWE, women with epilepsy (WWE) require a more comprehensive management strategy that takes into account reproductive health needs [39]. Indeed, optimal seizure control is recommended to ensure positive health and gestational outcomes for these women. However, most of the first-line AED routinely used in Africa (**Table 1**) may reduce the efficacy of hormonal contraceptives [40] or increase the risk for foetal malformations if taken during pregnancy [41]. Therefore, a tailored management approach is recommended for WWE and should include

Drug	Indication and frequency of use	Required dosage		Remark
		Children	Adults	
Phenobarbital	Recommended by WHO as first line AED for most seizure types, except absences; cheap and readily available [30, 32]. Used by 74.6% of PWE [33].	Given once or twice daily Starting dose: 2–3 mg/kg/day Maintenance: 3–6 mg/kg/day	Given once daily Starting dose: 60 mg/day Maintenance: 60–180 mg/day	Steady state reached after 14–21 days. Possible side effects: Drowsiness, skin rash, lethargy and hyperactivity in children, hepatic failure, Stevens Johnson syndrome
Carbamazepine	Indicated for focal seizures, and could be used in generalized convulsive seizures [31]. Used by 27.4% of PWE [33]	Given twice daily Starting dose: 5 mg/kg/day Maintenance: 10–30 mg/kg/day	Given twice daily Starting dose: 100–200 mg/day Maintenance: 400–1400 mg/day	Steady state reached in 8 days. Possible side effects: allergic skin reactions, bone marrow suppression with long-term use, blurred vision, diplopia, ataxia, nausea. Contraindicated in absences and myoclonus [31]
Phenytoin	Indicated for treating some generalized seizures and status epilepticus [34]. Used by 22.2% of PWE [33]	Given once/twice daily Starting dose: 3–4 mg/kg/day Maintenance: 3–8 mg/kg/day (max 300 mg daily)	Given once or twice daily Starting dose: 150–200 mg/day Maintenance: 200–400 mg/day	Possible side effects: drowsiness, ataxia, slurred speech, motor twitching and mental confusion, coarsening of facial features, hepatitis, gum hyperplasia, hirsutism, skin reaction including Stevens Johnson syndrome
Valproate	Broad spectrum anticonvulsant that can be used for both focal and generalized onset seizures. Specifically indicated for absence, atonic and myoclonic seizures [34]. Preferred drug for nodding seizures [35]. Used by 14.7% of PWE [33]	Given twice daily Starting dose: 5–10 mg/kg/day Maintenance: 15–30 mg/kg/day	Given twice daily Starting dose: 400 mg/day Maintenance: 400–2000 mg/day	Possible side effects: sedation, tremor, transient hair loss, increase in body weight, impaired hepatic function. Use in women of childbearing age is discouraged

Table 1.
Description of common first-line AEDs in resource-limited settings.

the following components: regular evaluation of the treatment regimen/dose and adjustments if needed; contraception and pre-conceptual counseling; psychosocial support and stigma-reducing interventions to improve their self-esteem and quality of life [42].

4. Public health interventions for epilepsy

The high epilepsy burden, unequaled treatment gap, and low quality of life of PWE in low-income settings have been a global health concern during the pass decades. Following the launching of the Global Campaign Against Epilepsy in the early 2000s by the International League Against Epilepsy (ILAE) and International Bureau for Epilepsy (IBE), a number of epilepsy demonstration projects which used a primary healthcare approach were launched in five developing countries: China, Senegal, Zimbabwe, Brazil, and Argentina [43, 44]. In 2015, epilepsy was acknowledged as a major public health problem during the 68th World Health Assembly, and participating countries engaged to step care up epilepsy care [45]. Eventually, the Mental Health Gap Action Programme (mhGAP) enabled the development of evidence-based guidelines for managing neurological conditions including epilepsy in resource-limited settings [30].

Outcomes from the various demonstration projects [46] as well as more recent studies in Guinea [28] and South Africa [47] are in favor of a community-based approach whereby local non-specialized staff and community health workers cater for the PWE. Phenobarbital, a cheap and available first-line AED, is the WHO's recommended molecule of choice for large scale epilepsy treatment [48]. Another important public health component in epilepsy is education and information campaigns, aimed at reducing the epilepsy-related stigma and its consequences on the quality of life of the PWE [32, 46].

5. Conclusion

Epilepsy remains a common neurological disorder with a wide clinical spectrum and a panoply of etiologies. Consensual diagnostic and therapeutic approaches have been established for epilepsy and they constantly evolve as more aspects of this condition are being uncovered by science. LMICs are the most affected by epilepsy, and should therefore be prioritized for interventions aimed at reducing the epilepsy burden.

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Conflict of interest

The author declares he has no conflict of interest.

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References

[1] World Health Organization. Epilepsy fact sheet [Internet]. 2019. Available from: https://www.who.int/news-room/fact-sheets/detail/epilepsy [Accessed: 12 March 2019]

[2] Beghi E. The epidemiology of epilepsy. Neuroepidemiology. 2020;**54**:185-191

[3] Fisher RS, Boas W van E, Blume W, Elger C, Genton P, Lee P, et al. Epileptic seizures and epilepsy: Definitions proposed by the international league against epilepsy (ILAE) and the International Bureau for Epilepsy (IBE). Epilepsia. 2005;**46**:470-472

[4] Fisher RS, Acevedo C, Arzimanoglou A, Bogacz A, Cross JH, Elger CE, et al. ILAE official report: A practical clinical definition of epilepsy. Epilepsia. 2014;**55**:475-482

[5] Falco-Walter JJ, Scheffer IE, Fisher RS. The new definition and classification of seizures and epilepsy. Epilepsy Research. 2018;**139**:73-79

[6] Scheffer IE, Berkovic S, Capovilla G, Connolly MB, French J, Guilhoto L, et al. ILAE classification of the epilepsies: Position paper of the ILAE Commission for Classification and Terminology. Epilepsia. 2017;**58**:512-521

[7] Thurman DJ, Beghi E, Begley CE, Berg AT, Buchhalter JR, Ding D, et al. Standards for epidemiologic studies and surveillance of epilepsy: Standards for epidemiologic studies and surveillance of epilepsy. Epilepsia. 2011;**52**:2-26

[8] Konanki R, Mishra D, Gulati S, Aneja S, Deshmukh V, Silberberg D, et al. INCLEN diagnostic tool for epilepsy (INDT-EPI) for primary care physicians: Development and validation. Indian Pediatrics. 2014;**51**:539-543

[9] Ngugi AK, Bottomley C, Chengo E, Kombe MZ, Kazungu M, Bauni E, et al. The validation of a three-stage screening methodology for detecting active convulsive epilepsy in population-based studies in health and demographic surveillance systems. Emerging Themes in Epidemiology. 2012;**9**:8

[10] Giuliano L, Cicero CE, Crespo Gómez EB, Padilla S, Bruno E, Camargo M, et al. A screening questionnaire for convulsive seizures: A three-stage field-validation in rural Bolivia. Romigi A, editor. PLoS One. 2017;**12**:e0173945

[11] Diagana M, Preux PM, Tuillas M, Ould Hamady A, Druet-Cabanac M. Dépistage de l'épilepsie en zones tropicales: validation d'un questionnaire en Mauritanie. Bulletin de la Société de Pathologie Exotique. 2006;**99**:103-107

[12] Fiest KM, Sauro KM, Wiebe S, Patten SB, Kwon C-S, Dykeman J, et al. Prevalence and incidence of epilepsy: A systematic review and meta-analysis of international studies. Neurology. 2017;**88**:296-303

[13] Ba-Diop A, Marin B, Druet-Cabanac M, Ngoungou EB, Newton CR, Preux P-M. Epidemiology, causes, and treatment of epilepsy in sub-Saharan Africa. The Lancet Neurology. 2014;**13**:1029-1044

[14] Beghi E, Hesdorffer D. Prevalence of epilepsy-an unknown quantity. Epilepsia. 2014;**55**:963-967

[15] Feigin VL, Nichols E, Alam T, Bannick MS, Beghi E, Blake N, et al. Global, regional, and national burden of neurological disorders, 1990-2016: A systematic analysis for the global burden of disease study 2016. The Lancet Neurology. 2019;**18**:459-480

[16] Fisher RS, Cross JH, French JA, Higurashi N, Hirsch E, Jansen FE, et al. Operational classification of

seizure types by the international league against epilepsy: Position paper of the ILAE Commission for Classification and Terminology. Epilepsia. 2017;**58**:522-530

[17] Fisher RS, Cross JH, D'Souza C, French JA, Haut SR, Higurashi N, et al. Instruction manual for the ILAE 2017 operational classification of seizure types. Epilepsia. 2017;**58**:531-542

[18] Dowell SF, Sejvar JJ, Riek L, Vandemaele KAH, Lamunu M, Kuesel AC, et al. Nodding Syndrome. Emerging Infectious Diseases. 2013;**19**:1374-1383

[19] Grinton BE, Heron SE, Pelekanos JT, Zuberi SM, Kivity S, Afawi Z, et al. Familial neonatal seizures in 36 families: Clinical and genetic features correlate with outcome. Epilepsia. 2015;**56**:1071-1080

[20] Brunklaus A, Dorris L, Ellis R, Reavey E, Lee E, Forbes G, et al. The clinical utility of an SCN1A genetic diagnosis in infantile-onset epilepsy: Clinical utility of SCN1A testing. Developmental Medicine and Child Neurology. 2013;**55**:154-161

[21] Carrizosa Moog J, Kakooza-Mwesige A, Tan CT. Epilepsy in the tropics: Emerging etiologies. Seizure. 2017;**44**:108-112

[22] Baraff LJ, Lee SI, Schriger DL. Outcomes of bacterial meningitis in children: A meta-analysis. The Pediatric Infectious Disease Journal. 1993;**12**:389-394

[23] Chesnais CB, Nana-Djeunga HC, Njamnshi AK, Lenou-Nanga CG, Boullé C, Bissek A-CZ-K, et al. The temporal relationship between onchocerciasis and epilepsy: A population-based cohort study. The Lancet Infectious Diseases. 2018;**18**: 1278-1286

[24] Lancaster E, Dalmau J. Neuronal autoantigens—Pathogenesis, associated disorders and antibody testing. Nature Reviews. Neurology. 2012;**8**:380-390

[25] Johnson TP, Tyagi R, Lee PR, Lee M-H, Johnson KR, Kowalak J, et al. Nodding syndrome may be an autoimmune reaction to the parasitic worm Onchocerca volvulus. Science Translational Medicine. 2017;**9**:eaaf6953

[26] Debacq G, Moyano LM, Garcia HH, Boumediene F, Marin B, Ngoungou EB, et al. Systematic review and meta-analysis estimating association of cysticercosis and neurocysticercosis with epilepsy. Flisser A, editor. PLoS Neglected Tropical Diseases. 2017;**11**:e0005153

[27] Siewe Fodjo JN, Dekker MCJ, Idro R, Mandro MN, Preux P-M, Njamnshi AK, et al. Comprehensive management of epilepsy in onchocerciasis-endemic areas: Lessons learnt from community-based surveys. Infectious Diseases of Poverty. 2019;**8**(11). Available from: https://doi.org/10.1186/s40249-019-0523-y

[28] van Diessen E, van der Maas F, Cabral V, Otte WM. Community-based rehabilitation offers cost-effective epilepsy treatment in rural Guinea-Bissau. Epilepsy & Behavior. 2018;**79**:23-25

[29] Caraballo R, Fejerman N. Management of epilepsy in resource-limited settings. Epileptic Disorders. 2015;**17**:13-18

[30] World Health Organization, editor. World Health Organization, Editors. mhGAP Intervention Guide for Mental, Neurological and Substance Use Disorders in Non-specialized Health Settings: Version 1.0. Geneva: World Health Organization; 2010

[31] Howlett W. Neurology in Africa: clinical skills and neurological disorders [Internet]. Tanzania; 2012. Available from: http://www.uib.no/filearchive/

neurologyinafrica_bora-complete-book.pdf

[32] World Health Organisation. Epilepsy in the WHO African Region: Bridging the Gap. Geneva: WHO; 2004

[33] Ibinda F, Odermatt P, Kariuki SM, Kakooza-Mwesige A, Wagner RG, Owusu-Agyei S, et al. Magnitude and factors associated with nonadherence to antiepileptic drug treatment in Africa: A cross-sectional multisite study. Epilepsia Open. 2017;**2**:226-235

[34] NICE. Epilepsies: Diagnosis and management [Internet]. National Institute for Health and Care Excellence; 2012. Available from: www.nice.org.uk/guidance/cg137 [Accessed: 03 December 2017]

[35] Idro R, Namusoke H, Abbo C, Mutamba BB, Kakooza-Mwesige A, Opoka RO, et al. Patients with nodding syndrome in Uganda improve with symptomatic treatment: A cross-sectional study. BMJ Open. 2014;**4**: e006476

[36] Hanaya R, Arita K. The new antiepileptic drugs: Their neuropharmacology and clinical indications. Neurologia Medico-Chirurgica (Tokyo). 2016;**56**:205-220

[37] O'Neill S, Irani J, Siewe Fodjo JN, Nono D, Abbo C, Sato Y, et al. Stigma and epilepsy in onchocerciasis-endemic regions in Africa: A review and recommendations from the onchocerciasis-associated epilepsy working group. Infectious Diseases of Poverty. 2019;**8**:34

[38] Kaddumukasa M, Kaddumukasa MN, Buwembo W, Munabi IG, Blixen C, Lhatoo S, et al. Epilepsy misconceptions and stigma reduction interventions in sub-Saharan Africa, a systematic review. Epilepsy & Behavior. 2018;**85**:21-27

[39] Stephen LJ, Harden C, Tomson T, Brodie MJ. Management of epilepsy in women. The Lancet Neurology. 2019;**18**:481-491

[40] Brodie MJ, Mintzer S, Pack AM, Gidal BE, Vecht CJ, Schmidt D. Enzyme induction with antiepileptic drugs: Cause for concern?: Enzyme induction with AEDs. Epilepsia. 2013;**54**:11-27

[41] Tomson T, Battino D, Bonizzoni E, Craig J, Lindhout D, Perucca E, et al. Comparative risk of major congenital malformations with eight different antiepileptic drugs: A prospective cohort study of the EURAP registry. The Lancet Neurology. 2018;**17**:530-538

[42] Menon S, Siewe Fodjo JN, Weckhuysen S, Bhwana D, Njamnshi AK, Dekker M, et al. Women with epilepsy in sub–Saharan Africa: A review of the reproductive health challenges and perspectives for management. Seizure. 2019;**71**:312-317

[43] ILAE/IBE/WHO. Global Campaign against Epilepsy [Internet]. 2003. Available from: https://www.who.int/mental_health/management/en/GcaeBroEn.pdf?ua=1

[44] Pal DK. China begins long march to epilepsy control. The Lancet Neurology. 2003;**2**:525

[45] WHO. Sixty-eighth World Health Assembly adopts resolution on epilepsy [Internet]. WHO. Available from: https://www.who.int/mental_health/neurology/epilepsy/resolution_68_20/en/ [Accessed: 21 July 2019]

[46] Wolf P, Reynolds E. International League Against Epilepsy – commissions, task forces and the Global Campaign Against Epilepsy. International League Against Epilepsy 1909-2009 A Centenary History [Internet]. Available from: https://www.ilae.org/7A4746E0-7C57-11E7-B3A0141877632E8F

[47] Wagner RG. The Burden of Epilepsy: using population-based

data to define the burden and model a cost-effective intervention for the treatment of epilepsy in rural South Africa [PhD thesis]. Umea, Sweden: Umea University; 2016. Available from: http://umu.diva-portal.org/smash/get/diva2:926968/FULLTEXT03.pdf

[48] Scott RA, Lhatoo SD, Sander JWAS. The treatment of epilepsy in developing countries: Where do we go from here? Bulletin of the World Health Organization. 2001;**79**:344-351