Epilepsy in Sub-Saharan Africa: Challenges of Management

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Mustapha Danesi

Historical note

The earliest detailed account of epilepsy can be found in the British Museum in London as part of *Sakikku* (meaning "all diseases"), a Babylonian text on medicine written over 3000 years ago. The Babylonians provided descriptions of many of the seizure types referrred to as *miqtu*, including what are now called "tonic-clonic seizures," "absences," "drop attacks," "simple and complex partial seizures," and "focal motor (Jacksonian)" or "gelastic" attacks.

Due to its dramatic intermittent nature, epilepsy has been shrouded in mysticism for many centuries. The Greeks considered epilepsy to be a "disease of the gods", believing that only the gods that could make someone unconscious, convulse and then recover completely from the attack. In 450 B.C., Hippocrates disputed this thinking, proposing that epilepsy was caused by abnormalities of the brain. During the time of Jesus Christ it was popularly believed that epilepsy was due to possession by a demon as illustrated in the bible story when Jesus Christ cast away the demon from an epileptic patient having a seizure. This supernatural view has dominated the thinking about epilepsy, and even now it has a deeply rooted negative social influence especially in the developing world.

In Medieval Europe, epilepsy was known as the falling sickness or the sacred disease and was often ascribed to possession by evil spirits. Later, it was generally considered to be a psychiatric condition, until a biological basis was seriously considered in the mid-19th century.

In Africa, the supernatural views of epilepsy still predominate. In many parts of Nigeria, epilepsy is thought to be due to possession by evil spirits. Moreover, it is popularly believed that epilepsy is contagious and acquired by contact with the saliva of an epileptic patient during a seizure. In Senegal, however, epileptic patients are regarded as "Spiritual Holy Men" and are revered or even worshiped. I have often wondered why epileptics are shunned in Nigeria, because one of the most effective ways a traditional medical practitioner or a sorcerer in Nigeria can demonstrate his power before a client is to "consult the ancestors" by going into "simulated epileptic seizures" and from this state to deliver a message from the ancestors. Christian spiritualists also go into "simulated epileptic seizures" to consult the "Holy Spirit" and equally emerge from this state to declare what the "Holy Spirit" has said.

The modern era of pharmacotherapy began with bromides in the 19th century. Other drugs, like phenobarbital (1912) and phenytoin (1938), came into vogue later. In the second half of the 20th century, remarkable progress was made in diagnostic facilities with structural and functional neuroimaging, video-telemetry, and magneto-encephalography. In recent decades several new drugs have been introduced and gained popularity. While some of them are now available in sub-Saharan Africa, most are either not available or too expensive.

Thus, the history of social attitudes to epilepsy in the developing world can be summarized as thousands of years of ignorance, superstition, and stigma, followed by a century of knowledge (not uniformly so). Knowing that seizures result from

sudden, excessive, abnormal electrical discharges from a set of neurons in the brain has done little to dispel the misunderstanding about epilepsy in most parts of the developing world where more than 70 per cent of sufferers remain untreated despite the availability of inexpensive anti-epileptic drugs.

The Burden of Epilepsy in Developing Countries

Introduction

Although the World Health Organization has made significant progress in defining the magnitude of the problem of epilepsy and identifying the likely etiological factors, our understanding of the epidemiology of epilepsy in developing countries is still incomplete. The problem is particularly compounded in areas where patients with epilepsy do not have access to physicians and neurologists and where diagnostic methods such as electroencephalography (EEG) and CT scan may not be available. Other difficulties include the following:

1. The diagnosis of epilepsy is not always straightforward and may require EEG confirmation.
2. The classification of epilepsy and epileptic syndromes has become complicated and poorly suited for field studies.
3. The definitions used vary in different studies; and the inclusion criteria are not always clear.

Information on the number of people with epilepsy is essential for the identification of needs and the planning of appropriate services in developing countries where the spectrum of causes for symptomatic epilepsy is different. Epilepsy services are not only scarce in developing countries, but the few services available are underutilized because patients are required to pay from their pockets.

Sub-Saharan Africa

Epidemiological studies in sub-Saharan Africa are not easily accessible to the scientific community. More than half of these studies have been published in regional journals that have very low distribution and are not indexed in the international databases. Methodological constraints and inconsistencies make epidemiological studies on epilepsy difficult to compare.[1] The lack of specialized personnel, particularly in neurology, and poor availability of diagnostic equipment means that the accuracy of diagnosis cannot be confidently ascertained.

Prevalence of Epilepsy

The prevalence of epilepsy in the United States is generally reported to be 5 to 10 per 1000 when only chronic epileptic conditions are considered.[2] Prevalence data show that epilepsy is two to three times more common in sub-Saharan Africa than in industrialized countries in non-tropical areas. The median prevalence found in the door-to-door studies was 15 per 1000 people.[3] In sub-Saharan Africa, the prevalence of epilepsy can be quite variable even in the same country. Studies in Tanzania and Nigeria have consistently found higher prevalence of epilepsy in rural than in urban areas using identical methodologies, further suggesting that infectious diseases may be an important etiological factor for epilepsy in the developing world. In two studies in Nigeria, Osuntokun et al using the same protocol, found a prevalence of 5·3 per 1000 in Igbo-Ora Town [4] and 37·0 per 1000 in Aiyété Village, 20 km away from Igbo-Ora [5]. This discrepancy, they explained, was due to better sanitary conditions and health care facilities in Igbo-Ora compared to Aiyete village, in particular in the prevention of neonatal infection and birth trauma.

Incidence

Generally in developed countries the incidence of epilepsy ranges from 24-53 per 100,000 persons-years[6,7] There are few incidence of studies in sub-Saharan Africa. In general, annual incidences found in these studies were higher :(64—156) per 100,000 persons- year.[8,9]

Possible reasons for the higher incidence in sub-Saharan Africa include: Poorer medical facilities, poorer general health, lower standard of living, higher rates of infections, especially from parasitic diseases (particularly neurocysticercosis), HIV, trauma, and perinatal morbidity.

Time Trends in incidence

In the developed countries, there has been a decline in the incidence of epilepsy in children under the age of 10 years and an increase in incidence in people above 60 years probably due to an increase in vascular causes such as stroke.[10] In sub-Saharan Africa, time trends have not been studied.

Risk Factors for Epilepsy

The relative contribution of each of the factors in a population is difficult to determine. Only a few studies applying case-control methodology have been done in sub-Saharan Africa. Two case-control studies from sub-Saharan Africa (Nigeria and Tanzania) showed a significantly high risk of long-term epilepsy after febrile seizures. In a case-control Study in Ibadan, Nigeria, Ogunniyi et al and Bademosi et al showed that childhood febrile seizure was strongly associated with epilepsy with an odds ratio of 11·0. [11,12] In a Tanzania study, the odds ratio was 2.9.[13] In a recent study, Ogunrin et al identified risk factors for epilepsy, there are febrile seizures (odds ratio 5.74), birth asphyxia (OR 6.87), CNS infections

(OR 3.38), and history of epilepsy in first degree relatives (OR 3.44). [14]

Aetiology of epilepsy in sub-Saharan Africa

The potential number of aetiological factors for epilepsy in developing countries is different, and many are preventable. Intracranial infections are of particular importance in this respect. Where simple preventive measures fail, the solution may lie in vaccination, eg, the control of epidemic meningococcal meningitis. Epilepsy and other long-term sequelae of intracranial infections can be minimized by early detection and prompt and adequate treatment.

Information regarding the causes of epilepsy has implications for decision-making about the development of locally relevant strategies for prevention and management, research goals, and education of primary health care workers and community physicians.

Aetiologically, the epilepsies are classified into four groups: idiopathic, symptomatic, cryptogenic, and progressive. The top four most frequently reported aetiologies of epilepsy—ie, trauma, central nervous system infections, perinatal risk factors, and cerebrovascular disorders—are preventable. In young children and adolescents, idiopathic epilepsies account for the majority of cases, although trauma and infection play a role. In a study in Lagos, Nigeria by Danesi et al, the commonest aetiological factor was childhood febrile seizures followed by head injuries, while two thirds of the patients had no identifiable aetiology.[15]

Perinatal Causes

The most common acquired causes of epilepsy in young infants are: perinatal hypoxia, birth trauma, metabolic disturbances,

congenital malformations of the brain, and infection. Perinatal complications increased the risk of epilepsy 4.5 times in Tanzania and 1.9 times in Burundi.

This is a subject of special interest in sub-Saharan Africa where most children are born at home without professional help. Obstetric injuries, neonatal hypoxia, and watershed cerebral ischaemia are common.[16] Multiparity, prematurity, and maternal infections worsen this situation. [17]

Head Injury

Road accidents are common in Africa owing to relatively poor traffic regulation and control. Lack of a consistent seat-belt policy and absence of a helmet law for riders are major contributors to head injury. Work-related injuries, fights among individuals, violent sports, and injuries from war also contribute to head injuries. The prevalence of epilepsy varies according to the severity of the injury (in a group of 250 patients with head injuries caused by gunshot wounds during the Nigerian civil war, 16.4 per cent had seizures) .[18]

Brain Tumours

Tumours are implicated in epilepsy in 1 to 10 per cent of cases in sub-Saharan Africa. This range is similar to that found in industrialized countries.[19] Absence of CT scans is a source of bias and many tumours are diagnosed only in advanced stages. In studies in Nigeria by Adamolekun et al and Ogunniyi et al, space-occupying lesions were found in 10 to12 per cent of the patients with epilepsy .[20, 21]

Cerebrovascular Disease

Brain lesions which persist after a stroke can also cause epilepsy. The management of risk factors for cerebrovascular disease, such as high blood pressure, is poor in sub-Saharan Africa. However, 1 to 42 per cent of patients with epilepsy have cerebrovascular disease, this variation is probably due to the paucity of neuroimaging devices. While a study in Nigeria by Ogunniyi et al, found no difference in the prevalence of cerebrovascular disease between patients with epilepsy and controls. [11]

Febrile Seizures

In sub-Saharan Africa a history of febrile seizures are common among people with epilepsy. Most febrile seizures occur in patients with malarial fever. The clinical importance of other infections in febrile seizures has also been pointed out. Febrile seizures are often severe in children and recur frequently. Studies from sub-Saharan Africa (Nigeria and Tanzania) showed a significantly high risk of long-term epilepsy after febrile seizures. [11, 12, 13]

Infections

Infections are common causes of epilepsy in sub-Saharan Africa. Epilepsy may occur in the course of a number of parasitic disorders, including neurocysticercosis, falciparum malaria, schistosomiasis, and paragonimiasis. Such infections may be responsible for the higher incidence of epilepsy in some parts of the tropical world. Seizures in patients with HIV can occur during opportunistic infections, including cryptococcosis, herpes simplex virus, toxoplasmosis, and tuberculosis. Cerebral toxoplasmosis has been reported to cause seizures in about 25 per cent of infected cases and the prevalence is much higher in patients with HIV. Human Immunodeficiency Virus can also produce seizures

through direct invasion of the CNS. [23,24] Bacterial meningitis (meningococcal) and encephalitis commonly cause epilepsy. Twenty-six of 144 children hospitalised in Yaounde (Cameroon) had long-term epilepsy. [25] In Sudan, epilepsy still occurred in 11 per cent of infants 3 years after meningococcal meningitis.[26] Tuberculous meningitis causes long-term epilepsy in 8 to14 per cent of patients. [27] In a study in Dakar, Senegal, 18 per cent of 3,327 patients with measles had epilepsy.[28] Parasites can cause seizures or long-term epilepsy by producing diffuse encephalitis or localized lesions. Laboratory or imaging tests are key in determining the specific incidence of epilepsy caused by each parasite. Neurocysticercosis is the most common acquired cause of epilepsy in resource-poor countries. This occurs when a human becomes the intermediate host for *Taenia solium* through the ingestion of eggs contained in human faeces.

Cysticercosis is caused by an infestation by the larvae of *Taenia solium* in pork. In Africa, except for the Muslim areas, there are still many regions where pigs are raised traditionally and where all conditions (particularly poor sanitation) are fulfilled for transmission of *T. solium* from pigs to humans and vice versa. *T solium* and cysticercosis are endemic in many countries in sub-Saharan Africa.[29,30]

A matched case-control study was recently done in the Kiremba community in Burundi (a region with endemic cysticercosis).[31] In this study, 324 cases with epilepsy and 648 controls were included. A positive association between cysticercal seropositivity and epilepsy was found after adjustment for other significant factors such as sex, poor sanitation, and past history of severe disease in childhood (adjusted odds ratio 4.1). Cysticercal seroprevalence was 35.1 per cent among the controls, making this region a hyperendemic zone for this disease. Cysticercosis is an eradicable disease.[32] Eradication of this parasite would result in

more than 50 per cent reduction in the prevalence of epilepsy in Kiremba

Genetic Factors

A family history of epilepsy is noted in 6 to 60 per cent of patients studied in sub-Saharan Africa, whereas only 5 per cent have such a history in the USA.[33] In Tanzania, studies found a complex transmission of epilepsy among the Wapagoro people.[34,35] In certain communities, consanguinity is common, even as high as 96 per cent among the Dogon in Mali [36]. Developing countries, especially those of sub-Saharan Africa can, however, make a great contribution in genetic research due to the availability of large family samples.[37.]

For example, in Senegal, Farnarier and Gueye are studying six large pedigrees from families with several cases of different forms of epilepsy. A thorough clinical and paraclinical examination will be coupled with genotypic results.[38]

Reported causes of seizures and epilepsy regarding the age of onset in sub-Saharan Africa (adapted from Genton, 1992 and reports from African teams).

0 – 4 months: Neonatal asphyxia; perinatal traumatism; infections; cerebral malformation; subdural haematoma; hypoglycaemia; hypocalcaemia; inborn errors of metabolism.

4 months – 2 years: Sequel to previous causes; infections; vascular causes; inborn errors of metabolism; West syndrome.

2 – 10 years: Sequel to previous causes; idiopathic generalized epilepsy; infections; post-traumatic epilepsy; intoxication; Lennox-Gastaut syndrome; inborn errors of metabolism: primary tumours.

0 – 20 years: Sequel to previous causes; idiopathic generalized epilepsy; post-traumatic epilepsy; intoxication including alcohol

and other drugs; infections; malformations; Lennox-Gastaut syndrome; inborn errors of metabolism, malformations, neurodegenerative disorders.

20–40 years: Sequel to previous causes; post-traumatic epilepsy; brain tumours; alcohol; infections; vascular diseases, tumours and abscesses, neurodegenerative disorders.

40 – 60 years: Tumours; alcohol; head trauma; infections; vascular causes; metabolic disorder.

> 60 years: Vascular causes and metabolic disorders primary and secondary tumours; neurodegenerative disorders; infections

Prognosis of Epilepsy in Sub-Saharan Africa

Mortality

Very little data is available on epilepsy mortality in sub-Saharan Africa. In particular, information on long-term follow-up in patients with epilepsy is scarce. In Ethiopia, the crude mortality in patients with epilepsy was 31.6 per 1000, twice the mortality rate estimated in people without epilepsy (16.4/1000).[39] This observation was based on 20 deaths in a population of 316 epileptic patients in two years. Epilepsy was the primary cause of death in nine patients (eight patients died from status epilepticus and one died from severe burns following a seizure). In Kenya, Snow and colleagues reported a mortality of 3.5 per 1000 in patients above 5 years; the primary cause of death seemed to be epilepsy in 77 per cent of deaths.[40] Jilek-Aall and Rwiza reported that patients with epilepsy had twice the mortality rate within the same age groups of the general population in Tanzania.[41] Death occurred in more than half of the patients, 10 years after the start of therapy. The researchers reported that 145 of 164 patients benefited from treatment, which significantly reduced the number of deaths due to epilepsy-related events. Many other deaths were

linked to the disadvantaged position of people with epilepsy in the community.

In Cameroon, Kamgno and co-workers found in 128 patients with epilepsy a six-time greater risk of dying than in controls, because most of the patients did not receive appropriate and regular treatment.[42]

Seizure Remission

In developed countries, hospital-based intervention studies have reported a one-year remission rate between 58 per cent and 95 per cent when treatment is started early. In a study of epileptic patients attending the outpatient clinic in Lagos, Danesi et al found that only 36.5 per cent in all patients, 60 per cent of patients with generalized epilepsy and 24 per cent of patients with partial epilepsies were seizure-free after two years of treatment.[43] Ogunniyi et al found 30 per cent remission in a study at Ibadan.[44] Factors contributing to this low remission rate were the poor treatment compliance and a history of six or more seizures before treatment onset. Ogunniyi and Osuntokun evaluated the effectiveness of anticonvulsant drugs in Nigerian epileptics and found complete seizure control in 17 per cent; more than 50 per cent reduction in 50 per cent; and poor control in 33 per cent. Factors associated with good controls are infrequent seizure and monotherapy.[45]

Spontaneous Remission

Spontaneous remission can occur in untreated epileptic patients. In a community survey in Lagos, Danesi et al found spontaneous remission in up to 48 per cent of patients with a history of generalized epilepsy, although much lower in patients with partial epilepsy. Watts found a high spontaneous and permanent remission rate in Malawi in untreated patients.[46] In view of these

results, other studies are required, to investigate the issue of remission in such a context.

Effects of Early Anti-epileptic Drug Treatment on Prognosis

Available studies in sub-Saharan Africa refute the notion that late treatment reduces the likelihood of good responses to anti-epileptic drugs. In a Kenyan study, many had chronic epilepsy lasting more than five years and 38 per cent had frequent seizures; 81 per cent were drug naïve, yet 58 per cent became seizure free on treatment and 26 per cent had substantial seizure reduction. These findings are similar to those reported for newly diagnosed epilepsy in the developed world. [47]

Clinical Features of Epilepsy

Classification and Clinical Manifestations

The International League Against Epilepsy (ILAE) defines an epileptic seizure as "a transient occurrence of signs and/or symptoms due to abnormal, excessive or synchronous neuronal activity in the brain". The clinical manifestations are extremely variable and depend on the cortical areas involved. Epileptic seizures are usually self-limiting, lasting a minute or two, and may be followed by a period of post-ictal cerebral depression, manifested clinically as diffuse or localized neurological deficits.

The first step in the treatment of epilepsy is an accurate classification of seizure type and epilepsy syndrome. The international classification of epileptic seizures and epilepsy syndromes are accepted worldwide, providing a standard system for describing seizures and epilepsies.

Seizures are the hallmark symptom of epilepsy. An epileptic seizure is a transient clinical event due to abnormal neuronal activity of the brain.

Epilepsy is characterized by:

1. At least one epileptic seizure
2. An enduring predisposition to epileptic seizures; with associated cognitive, psychological and social consequences
3. An enduring predisposition to epileptic seizure with a higher than 50 per cent chance of seizure recurrence without AED treatment

Classification of Seizure Type

The 1981 classification is the current accepted classification of seizures but was modified in 2001. One of the main changes is the recognition of seizure type as a "diagnostic entity". When an epilepsy syndrome diagnosis cannot be made, seizure type can be used to provide information useful for the determination of aetiology, choice of treatment and prognosis.

Generalized Seizures

Generalized seizures begin simultaneously in widespread brain regions in both hemispheres. Consciousness is usually impaired. Motor manifestations are bilateral and synchronous. Auras, by definition, do not occur before generalized seizures; however, prodromal symptoms due to systemic disturbances that herald the onset of generalized seizures may be reported.

Generalized seizures are defined as "originating at some point within and rapidly engaging, bilaterally distributed networks. Such bilateral networks can include cortical and sub-cortical structures, but do not necessarily include the entire cortex.

Absence Seizures

Typical absence seizure show abrupt onset and offset of loss of awareness, lasting 5 to 30 seconds, without post-ictal confusion. It is characterized by blank starring, sometimes with slight upward eye deviation and repetitive blinking. A typical seizure in childhood absence epilepsy last 5 – 15 seconds and may occur hundreds of times a day. In juvenile absence epilepsy, absence is slightly longer and occurs less frequently (once a week to once a month). It may be confused with complex partial seizures if automatisms are present. Absence of post-ictal confusion may aid diagnosis. The

hallmark EEG finding in typical absence seizure is the generalized 3 cycles per second spike and slow wave complexes.

Atypical Absence Seizures

Atypical absence seizures occur in symptomatic generalized epilepsies. Onset and offset are less abrupt than in typical absence. Associated clinical features such as atonia, myoclonic jerks of the face or mouth, tonic stiffening, and automatisms are more frequent and more pronounced than in typical absence seizures. Seizure offset is gradual and post-ictal confusion occurs. EEG shows generalized irregular spike and wave complex at repetitive rates slower than 3Hz

Myoclonic Seizures

Myoclonic seizures are brief generalized jerks of arms and/or legs, often occurring in clusters mostly within 1 to 2 hours after awakening. During brief myoclonic jerks, consciousness is not impaired. The arms are more commonly involved, frequently resulting in dropping objects from the hands. When the legs are involved, myoclonic jerks may cause falls.

The EEG correlates of myoclonic jerks is a high-voltage generalized polyspike or polyspike and wave discharges. Myoclonic seizures are the hallmark of juvenile myoclonic epilepsy, but may also occur in other types of primary or symptomatic generalized epilepsy.

Myoclonic Absence Seizures

Myoclonic absence seizures show rhythmic clonic jerking at frequencies of 2 Hz to 4 Hz, coinciding with generalized polyspike and wave discharges. They typically last 5 to 10 seconds. In contrast to myoclonic seizures which have no impairment of consciousness, myoclonic absence seizures are characterized by brief lapses of awareness.

Tonic Seizures

Tonic seizures are characterized by sustained contractions of axial and limb muscles lasting 5 to 20 seconds. Limbs may be fixed in either flexor or extensor postures. Upward deviation of the eyes and extension of the neck may occur. Lateral head or eye movements can also occur. Consciousness is impaired during the seizure, but post-ictal confusion is brief. Tonic seizures occur in clusters ,usually during sleep. The EEG during tonic seizures shows generalized low-voltage paroxysmal fast activity at frequency greater than 10 Hz, usually with diffuse attenuation of EEG voltage. Tonic seizures occur characteristically in Lennox – Gastaut syndrome.

Generalized Tonic-Clonic Seizures (GTCS)

Formerly called *grand mal*, GTCS begin with tonic stiffening and loss of awareness, progress to generalize clonic jerking, and are followed by post-ictal obtundation. Patients may describe a vague

prodrome of irritability, headache and mood changes for hours to days before a seizure, but no specific aura is present. During the episode, the patient may bite his/her tongue as the jaw clenches. Autonomic symptoms such as tachycardia, hypertension and profuse salivation occur. GTCS last 1 to 2 minutes. At the end of the seizure, urinary incontinence may occur as sphincter muscles relax. During the post-ictal phase, the patient is stuporous or obtunded, with deep sonorous respiration. Consciousness is gradually recovered, but patient may remain confused for hours. Post-ictal headache and diffuse myalgia is common. Ictal EEG shows initial generalized low voltage rhythmic fast activity in the beta frequency ranges. This gradually decreases to 10 Hz and increases in amplitude during the tonic phase. Much of the seizure can be partially or completely obscured by muscle artifact. During the clonic phase, the EEG shows bouts of generalized spike and wave activity, alternating with severe diffuse background alteration.

Atonic Seizures

Atonic seizures are characterized by a brief diffuse loss of tone in postural muscles lasting 1 to 2 seconds. Mild seizures may cause a head drop or loss of tone in the limbs, causing the patient to drop objects. More severe atonic seizures, termed "drop attacks", result in a loss of all tone and a sudden collapse or fall to the ground, resulting in injuries. Atonic seizures last less than 5 seconds and have no post-ictal confusion. They are characteristic of symptomatic generalized epilepsies such as the Lennox-Gastaut syndrome. The EEG of atonic seizures is very variable, including patterns of diffuse alternation, high voltage generalized polyspike and wave discharges, high voltage slow waves or low voltage paroxysmal fast activities.

Epileptic Spasms

Epileptic spasms (previously called infantile spasm) are sudden flexion, extension or mixed flexion – extension movements of the trunk and proximal muscles. These are more sustained than myoclonic jerks, but shorter than tonic seizures, lasting 1 to 2 seconds. Facial grimacing, and upward eye deviation may occur with the spasms.

Spasms often occur in clusters, recurring every 5 to 10 seconds up to several minutes to hours. Epileptic spasms are most characteristic of West syndrome.

Focal Seizures (Partial Seizures)

Focal epileptic seizures are viewed as "originating within networks limited to one hemisphere. They may be discretely localized or more widely distributed. For each seizure type, ictal onset is consistent from one seizure to another, with preferential propagation patterns that can involve the contralateral hemisphere. In some cases, however, there is more than one network, and more than one seizure type, but each individual seizure type has a consistent site of onset.

In the 1981 classification, partial seizures are further divided into simple partial seizures, complex partial and secondarily generalized tonic clonic seizures. During simple partial seizures, consciousness is not impaired, but consciousness is impaired in complex partial seizures. Secondarily generalized tonic-clonic seizures represent spread of the ictal discharge from a restricted focus to the entire brain. The new proposed classification does not distinguish between simple and complex partial seizures; rather it divides seizures into those in which the ictal discharge remains localized and those in which it propagates to distant ipsilateral or contra lateral brain regions. It also attempts to separate seizures beginning in the neocortex from those starting in the limbic region.

The new proposed classification addresses the problem of accurately identifying lateralizing or localizing features, which could not be done by straight forward loss of awareness.

In the new classification, focal seizures can be classified by site of onset (hippocampal versus neocortical) and extent of spread (local, regional, bilateral or secondarily generalized). Focal seizure with local onset and limited spread show elementary motor signs, elementary or experiential sensory symptoms or signs. Focal seizures with contralateral spread involve complex motor movements (automatisms or bilateral posturing), sometimes with impairment of consciousness. However, the older classification was quite helpful in concisely communicating when patients have altered awareness during a seizure, indicating the risk for injury from automatic or confused behaviour.

Simple Partial Seizures

Clinical Features:

- No alteration of consciousness; no amnesia, focal symptoms or signs.
- Simple partial seizures usually arise from a fairly restricted anatomical region of the brain usually a single lobe or hemisphere.
- The symptoms and signs of the seizures reflect the functions of the brain region involved in the ictal discharge.
- Simple partial seizures are usually brief in duration lasting approximately 15 seconds to 2 minutes.
- Interictal EEG may show epileptiform discharges, often localized to the lobe of seizure origin, but can be normal.

Complex Partial Seizures

Complex partial seizures (CPS) account for 40 per cent of partial seizures. CPS of temporal lobe origin is the most common, accounting for about 70 per cent; about 20 per cent are from the frontal lobe; and 10 per cent divided between the parietal and occipital lobe.

Aura: Many complex partial seizures are preceded by a simple partial seizure or an aura which may be helpful in localizing the ictal onset zone. An aura is usually short-lived lasting few seconds.

Altered consciousness: This may be preceded by an aura, or may occur without warning. The altered consciousness takes the form of an absence and motor arrest, during which the patient is motionless and inaccessible. There is sometimes no outward sign; the patient eyes may appear vacant or glazed.

Automatisms: Automatism occurs during or after impairment of consciousness. It is defined as "a more or less coordinated involuntary motor activity occurring during the state of clouding of consciousness, either in the course of, or after an epileptic seizure, usually followed by amnesia for the event". Automatisms have no localizing value and should be distinguished from simple post-ictal confusion, hysterical fugues, acute states of confusion and sleep waking.

Automatisms are usually divided into:

1. **Oro-akinentary:** oro-facial movement such as chewing lip smacking, swallowing etc.
2. **Mimetic:** Acting out the patient emotional state
3. **Gestural:** Fiddling movements with hands tapping, rubbing, patting, ordering and tidying. Complex movement such as undressing.
4. **Ambulatory:** Walking, running, wondering around carrying out purposeful movements.

5. **Vocal/Verbal:** Humming, whistling, and grunting. Repetitive utterances of words or sentences.
6. **Hypokinetic:** Behavioural arrest, motionless limbs
7. **Hyperkinetic:** large amplitude movements of proximal limbs such as thrashing, rocking, pedaling, pelvic thrashing
8. **Gelastic:** Burst of laughter without any cause
9. **Dacrystic:** Burst of crying without sadness.
10. **Aggressive action:** Violent behaviour sometimes occurs in automatism especially if the patient is restrained. The violent actions are never premeditated, never remembered, never highly coordinated or skilful or goal directed. There is usually total amnesia for the event of automatism.
11. **Complex partial seizures:** These vary considerably in duration (from 3 seconds to 28 minutes). The scalp EEG is normal in 10-30 per cent during seizure. In the rest, runs of fast activity, localized spike and wave complexes, or sharp waves or slow waves may occur, or the EEG may simply show flattening (disynchronization).

Secondarily Generalized Seizures

Secondarily generalized tonic-clonic seizures (GTCS) represent a spread from a limited focus to the entire brain. They may begin as simple partial seizures with subsequent generalizations or progress through a sequence from simple to complex partial to generalized seizure. In some cases, particularly in frontal and parietal lobe seizures, the spread of the ictal discharge is rapid, and localizing or lateralizing features may be present.

Classification of Epilepsy

The International League Against Epilepsy (ILAE) has defined epilepsy as "a disorder of the brain characterized by an enduring predisposition to generate epileptic seizures and by the neurobiological, cognitive, psychological, and social consequences of this condition.

A definition of epilepsy requires the occurrence of at least one epileptic seizure, where seizures reflect the existence of an enduring epileptogenic disturbance with the potential to generate further seizures. Reactive (acute symptomatic, provoked) seizures due to transient insults of an otherwise normal brain that resolve spontaneously, or are successfully treated, do not warrant a diagnosis of epilepsy.

The International Classification of Epilepsies and Epileptic Syndromes divides epileptic disorders into those due to inherited epileptogenic cerebral dysfunction (primary or idiopathic epilepsy) and those due to specific structural abnormalities, which may be genetic (such as tuberous sclerosis) or acquired (secondary or symptomatic epilepsy).

When a disorder is presumed to be secondary epilepsy, but the specific underlying pathological substrate has not been identified, it is referred to as cryptogenic. Epileptic disorders are further sub-classified as partial or generalized, depending on whether the underlying disturbance is believed to be localized to a part of the brain or diffusely distributed over both hemispheres.

This classification also recognizes undetermined epileptic disorders when there is insufficient information for classification and disorders associated with reactive seizures, referred to as situation-related epilepsies. Disorders characterized by ictal events that are induced by specific stimuli (eg, photogenic epilepsy, reading epilepsy, startle epilepsy) are referred to as reflex epilepsies. In a study in Lagos, Danesi et al, found that

partial epilepsies constituted 75 per cent of the patients while 25 per cent had generalized epilepsies, similar to the pattern of epilepsies found in other parts of the world.[27]

The 2006 ILAE report also developed criteria for identifying specific epilepsy syndromes as discrete diagnostic entities, which include the epileptic seizure type associated with it, age of onset, the progressive nature of the disorder, interictal EEG abnormalities, associated interictal signs and symptoms, pathophysiological mechanisms, anatomical substrates, aetiologic categories, and genetic basis. The most recent ILAE report replaced the terms "idiopathic," "symptomatic," and "cryptogenic" with the following:

1. Genetic: These disorders are "the direct result of a known or presumed genetic defect(s) in which seizures are the core symptom of the disorder, but the possibility that environmental factors contribute to expression of the disease is not excluded."

2. Structural-metabolic: In these conditions, "there is a distinct other structural or metabolic condition or disease that has been demonstrated to be associated with a substantially increased risk of developing epilepsy in appropriately designed studies." These disturbances can be acquired or genetic (eg, tuberous sclerosis).

3. Unknown cause

With respect to the classification of the epilepsies, this report recommends that the dichotomy of focal versus generalized be abandoned. Furthermore it recognizes that syndromes can be characterized according to many different features, including:

- Age of onset
- Cognitive and developmental antecedents and consequences
- Motor and sensory examinations
- EEG features

- Provoking or triggering factors
- Patterns of seizure occurrence with respect to sleep

Electro Clinical Epilepsy Syndromes

Arranged by Age of Onset

Neonatal period

1. Benign familial neonatal epilepsy (BFNE)
2. Early myoclonic encephalopathy (EME)
3. Ohtahara syndrome

Infancy

1. Epilepsy of infancy with migrating focal seizures
2. West syndrome
3. Myoclonic epilepsy in infancy (MEI)
4. Benign infantile epilepsy
5. Benign familial infantile epilepsy
6. Dravet syndrome
7. Myoclonic encephalopathy in non-progressive disorders

Childhood

1. Febrile seizures plus (FS+) (can start in infancy)
2. Panayiotopoulos syndrome
3. Epilepsy with Myoclonic Atonic (previously Astatic) seizures
4. Benign epilepsy with centro-temporal spikes (BECTS)
5. Autosomal-dominant nocturnal frontal lobe epilepsy (ADNFLE)
6. Late-onset childhood occipital epilepsy (Gastaut type)
8. Epilepsy with myoclonic absences

9. Lennox-Gastaut syndrome
10. Epileptic encephalopathy with continuous spike-and-wave during sleep (CAWS)
11. Landau-Kleffner syndrome (LKS)
12. Childhood absence epilepsy (CAE)

Adolescence-Adult

1. Juvenile absence epilepsy (JAE)
2. Juvenile myoclonic epilepsy (JME)
3. Epilepsy with generalized tonic-clonic seizures alone
4. Progressive myoclonus epilepsies (PME)
5. Autosomal dominant epilepsy with auditory features (ADEAF)
6. Other familial temporal lobe epilepsies

Less specific age relationship

1. Familial focal epilepsy with variable foci (childhood to adult)
2. Reflex epilepsies
3. Distinctive constellations
4. Mesial temporal lobe epilepsy with hippocampal sclerosis (MTLE with HS)
5. Rasmussen syndrome
6. Gelastic seizures with hypothalamic hamartoma
7. Hemi convulsion-hemiplegia-epilepsy

Epilepsies that do not fit into any of these diagnostic categories can be distinguished firstly on the basis of the presence or absence of a known structural or metabolic condition (presumed cause), and then on the basis of the primary mode of seizure onset (generalized vs. focal).

Clinical Consequences of Epilepsy (Interictal morbidity)

Cognition: It has long been recognized that epilepsy can be associated with cognitive impairment. Even when overt structural abnormalities are not identified, children with epilepsy do not perform as well on intelligence tests than age-matched controls. The biggest impact of seizures on cognition is through post-ictal effects, possibly in the disruptive influence of epileptic discharge on long- term potentiation involved in learning. In a study of social problems of adolescent and adult Nigerian epileptic patients, Danesi et al found that among those attending school, epilepsy affected school performance in 75.9 per cent with 43.1 per cent performing below average and 32.8 per cent performing very poorly.[48] Dr. Ogunrin et al, found cognitive impairment of short-term memory, psycho-motor speed and sustained attention in epileptic patients.[49] Sunmonu et al showed that patients with epilepsy have significant cognitive impairment compared to controls.[50]

Mood disorders: Disorders of mood are commonly associated with epilepsy. Depression has been linked with epilepsy. Peri-ictal lowered mood is a well-known problem with prolonged depressive mood swing recorded. Many studies in the past using various types of depressive assessment scales all found that patients with epilepsy have had higher depression scores than controls. In a recent study in Lagos by our unit, Okubadejo et al, using Zung Depressive Scale, found depression in 26 per cent of the epileptic patients compared to 9.7 per cent of controls.[51]

Personality disorders: Personality disturbances are the most frequent psychiatric abnormalities reported in epileptic patients. Again the concept of "epileptic personality" is the most controversial concept in the field of epileptology. Some authors

have described a syndrome of personality change caused by excessive discharges in the limbic system. This contains most of the features of the 'epileptic personality' described by 19th and early 20th century authors, such as emotional instability, hypo-sexuality, hyper-religiosity and a tendency to adhere to each thought, feeling and action: the so called thought viscosity.

Menstruation: many women link occurrence of epileptic seizures to their menstrual period. The prevalence of Catamenial epilepsy is highly variable. Changes in hormonal concentration with oestrogen being pro-convulsant and progesterone being anti-convulsant have been considered as contributory factors.

Fertility: Fertility is reduced in women with epilepsy. Women with epilepsy have higher rates of reproductive and endocrine disorders that expected. Libido is reduced in both men and women

Social Consequences of Epilepsy in sub-Saharan Africa

Stigma: The social stigma attached to epilepsy can be traumatizing. Epilepsy is still believed by many Nigerians to be due to possession by evil spirits. Many people believe that epilepsy is contagious and can be transmitted by saliva of the patient having a seizure. These beliefs cause very unfavourable and negative attitudes towards epileptic patients. In a study among Nigerians Danesi et al found that a larger percentage of epileptic patients felt stigmatized by the condition. Many of them were unwilling to disclose their epilepsy to others. Others were in denial, refusing to even accept that they have epilepsy, even though they were taking regular medication.[52]

School performance: Although in general, over 60 per cent of children with epilepsy have normal intelligence, they appear to be at risk of various learning and behavioural disabilities. They have several cognitive deficits including memory deficits, attention

deficit, impaired problem solving and higher order cognition function.

Other factors contributing to low school performance relate to poor parental attitude, social and cultural circumstances and the child's self-esteem. Many parents frequently withdraw their children prematurely from school. Some teachers may send a known epileptic child away from school "to prevent the epileptic child infecting other children with epilepsy". In a study of school teachers in Lagos Nigeria, Danesi et al found that many of them had wrong beliefs about epilepsy and unfavourable attitudes towards epileptic school children.[53]

Employment: In a study in Lagos, Danesi et al found that many epileptic patients were employed despite the unfavourable attitudes of employers towards epilepsy. However, many of them would not admit to the diagnosis of epilepsy and therefore did not disclose their epilepsy to their employers. Because of this, they did not suffer discrimination by employers but many of them tended to do jobs that were dangerous for epileptic patients such as driving motor vehicles, operating machines in the factory, working at heights etc. [54]

Management of Epilepsy

Diagnostic work-up

The EEG is the most important diagnostic test for epilepsy. The pattern and location of inter-ictal epileptiform abnormalities not only help to make a diagnosis of epilepsy but also help to characterize the type of epileptic disorder or epileptic syndrome. The inter-ictal EEG alone, however, is not sufficient because 10 per cent to 20 per cent of patients with epilepsy do not demonstrate interictal epileptiform EEG abnormalities, whereas 2 per cent to 3 per cent of patients without epilepsy may show these abnormal transients. In a recent study in Lagos, Aina et al, found that 54.19

per cent of a cohort of epileptic patients who had EEG had interictal epileptiform activities in their first study while 30.4 per cent had normal EEG tracing.[55] Further yield can be obtained by repeat EEG or by one or more forms of activation methods. A well-known activation method is hyperventilation which elicits spike and wave discharges in patients with absence epilepsy. Another activation method is intermittent photic stimulation which induces spike and wave discharges called photo paroxysmal discharges (PPD). PPD usually occur in 5 per cent of epileptic patients in temperate countries but much less in tropical countries. In a study in Nigeria, Danesi and Oni found that PPD is rare in Nigerian patients with grand mal (1.24 per cent) compared to British patients (10.4 per cent).[56] The reason for this was thought to be due to the higher amount of sunshine in Nigeria compared to Britain. The relationship to sunshine was confirmed in a study by Danesi of the same group of British patients who had lower incidence of PPD in summer compared to winter.[57] A relatively lower incidence of spike and wave discharges was also found among the Nigerian patients compared to British patients. The implication of the rarity of PPD among the Nigerian patients is that the hazards of visual display unit of computers or video game to epileptic patients and their tendency to cause photosensitive epilepsy are thus much less in tropical region of sub-Saharan Africa.

A definitive diagnosis of epilepsy can be made if a seizure occurs during an EEG recording and electrographic ictal discharges can be correlated with habitual clinical signs and symptoms. Some types of ictal events can be precipitated in the EEG laboratory when necessary, or occasionally occur spontaneously during routine EEG testing, but continuous long-term EEG recording with video monitoring is the most effective way to evaluate habitual seizures.

Long-term monitoring for epilepsy is commonly used for differential diagnosis, and for identifying candidates for surgical treatment. When precise localization of a resectable epileptogenic region is required for surgical resection, long-term monitoring can involve the use of intracranial depth or cortical surface electrodes. Long-term monitoring for epilepsy is not available in most countries of sub-Saharan Africa.

Routine neurological and laboratory examinations are useful for identifying an underlying treatable cause of epilepsy. Unless an unequivocal diagnosis of primary epilepsy is made, the use of CT or MRI is appropriate to look for a structural cerebral lesion. MRI is the structural imaging procedure of choice, except for lesions where small calcifications are expected. Neuropsychological testing is useful for characterizing functional deficits for psychosocial prognosis and rehabilitation. Localizing information may also be obtained from these tests if surgical resection is contemplated.

Drug Treatment of Epilepsy

Initiation of Anti-epileptic Drugs

Anti-epileptic drug therapy should only be started after the diagnosis of epilepsy is confirmed. It is generally recommended after a second epileptic seizure. Anti-epileptic drug treatment should be considered

- After a first unprovoked seizure if the individual has a neurological deficit
- If the EEG shows unequivocal epileptic activity
- If the individual and/or their family consider the risk of having a further seizure unacceptable
- If brain imaging shows structural abnormality.

Before initiating therapy a full explanation to the patient of the risks and benefits of AEDs, and the need for regular drug compliance and long term-nature of therapy must be carried out.

Drug Treatment Strategies

The goal of therapy is to achieve complete seizure control with a single drug taken once or twice a day, without side-effects. It is most useful to formulate a treatment plan at the time of a patient's initial evaluation. The following steps are useful.

1. Any precipitating factors such as fever, excessive fatigue, alcohol and drug abuse etc, should be identified and the patient counselled about their avoidance.
2. The reason for instituting AED treatment, the expectations, limitation and the need for regular tablet taking should be explained.
3. It is particularly necessary to explain that AEDs do not provide a cure for epilepsy and have to be taken for a long time, usually many years, but in 70 to 80 per cent of patients seizures are controlled.
4. AEDs have to be taken regularly, and omitting doses raises the likelihood of further seizures occurring.

Patients should be started on a small dose of one of the first line AEDs recommended for their seizure type. The dose should be gradually increased until seizure remission is achieved.

As a guide the serum level of phenytoin may be particularly useful; serum levels of carbamazepine, phenobarbital or ethosuximide may be moderately helpful but serum levels of valproate is of very little use.

In an emergency situation, when a full and rapid anti-epileptic treatment is required, commencement of the full dose, and for phenytoin and barbiturates a loading dose, is necessary. In the

non-acute situation it is generally best to introduce an AED at a low dose and to increase over several weeks to the anticipated maintenance dose. If seizures continue it is appropriate to increase doses gradually up to the maximum tolerated. If patient does not have further seizures during the phase of drug introduction, it is customary to continue treatment at a lower dose.

If seizures continue despite a maximally tolerated dose of a first line AED, it should be determined whether or not the patient is taking the prescribed drug by non-confrontational enquiry If there is evidence of compliance another first line drug for that patient seizure should be commenced and built up to optimum dose if the first drug is ineffective and the first drug then be withdrawn. The dose of the second drug should be adjusted to optimum like initial agent.

If the seizures continues despite a maximally tolerated dose of all individual first-line drugs, the next step is to try a combination of two first line drugs for that seizure type e.g. ethosuximide and sodium valproate for absence or carbamazepine and sodium valproate for partial seizures. There is 10–15 per cent chance of the therapy controlling the seizures when monotherapy fails.

Seizure Type and First-line or Second- line AEDs

1. Generalized tonic-clonic seizure: phenytoin, valproate, lamotrigine, topiramate, levatiracetam.
2. Absence seizure: ethosuximide, valproate. Second choice: lamotrigine, topiramate, clonazepam. To be avoided: carbamazepine, gabapentin.
3. Myoclonic seizure: valproate second choice: clonazepam, lamotrigine, to be avoided: carbamazepine, gabapentin, phenytoin.

4. Atonic seizure: First choice: valproate, lamotrigine. Second choice: topiramate, clonazepam. To be avoided: carbamazepine, phenytoin.
5. Partial seizures with or without generalization: carbamazepine, valproate, phenytoin, phenobarbital.

Monotherapy and Polytherapy

Combination therapy was in vogue in the 1950s and 1960s. In the 1970s and 1980s evidence accrued for the advantage of monotherapy. Studies showed that monotherapy is associated with seizure control in 80 per cent of patients while combination of two drugs gives only 10 – 15 per cent additional improvement. Advantages of monotherapy include: simpler regimens, easier compliance , higher doses are tolerated with more effectiveness and less adverse effects. It minimizes long-term toxicity and no interactions between AEDs and less teratogenic effect. When two AEDs are combined, it is likely to be more helpful to combine two AEDs that have a different mode of action than agents that act in similar ways. There has been some work on the possibility of synergistic anti-epileptic effects of some combination of AEDs, leading to enhanced therapeutic index. For example, it has been suggested, that a combination of carbamazepine and sodium valproate has a better therapeutic index than carbamazepine and phenobarbital.

Anti-epileptic Drug Interaction

Drug interaction involving anti-epileptic drugs can cause serious morbidity and mortality if not anticipated and managed properly. To a large extent these interactions occur through an alteration of the pharmacokinetic parameters of one of the drugs: through the inhibition and/or induction of the hepatic enzymes. These enzyme systems are the P450 enzyme, glucuronyl transferase and epoxide

hydrolases. Another important pharmacokinetic interaction is the displacement of the drug from its protein binding sites in blood. Interactions among AEDs can lead to toxicity or to loss of antiepileptic activity.

Special Issues in the Management of Epilepsy

Below are useful guidelines in management of epilepsy which can be given by answering the following questions regarding Special Treatment Issues in epilepsy

1. What is the type of seizure or epilepsy?

Several of the newer and older AEDs can exacerbate minor seizures associated with idiopathic or symptomatic generalized epilepsy such as absence or myoclonic seizures. These include carbamazepine and gabapentin. Lamotrigine occasionally exacerbates myoclonic seizures. Therefore these drugs should be confined to patients with partial epilepsy. The various drugs used for different seizures types have been stated previously.

2. What are the cost constraints?

New AEDs are more expensive than those of the first generation drugs. Patients with limited financial resources may be limited to first generation AEDs. Because of this, new AEDs have not been popular in sub-Saharan Africa. The most effective and least costly drugs are encouraged.

3. Is this the first anti-epileptic drug?

The choice of initial therapy is critical as many patients will remain on this therapy for years and therefore it should be well tolerated and reasonably safe. Once individuals become seizure free they may be unwilling to attempt a change of therapy even if the original medication has side-effects.

4. Are there specific health issues that reduce the suitability of certain drugs?

Some patients may be poor candidates for certain drugs. Patients who develop a hypersensitivity rash to two or more AEDs, should ensure that the next drug has a low risk of rash. Sodium valproate should be avoided in patients with hepatic dysfunction.

5. Are there specific health Issues that enhance the suitability of certain drugs?

Carbamazepine may improve some behavioural disorders like depression; topiramate may be useful in obese patients.

6. Which drugs are safe for women who are of child-bearing age?

Several key issues arise when the patient to be treated is female. Hepatic enzyme inducers such as phenytoin, carbamazepine; phenobarbital alter the clearance of compounds metabolized through the liver, such as oral contraceptives. When used in early pregnancy, teratogenicity is a risk. Recent studies have shown an increased risk of teratogenicity associated with sodium valproate when compared to other AEDs. Therefore the drug should be avoided if the patient is a woman of child bearing age.

6.1 Hormonal contraception

Anti-epileptic drugs that induce the activity of hepatic microsomal enzymes (phenobarbital, phenytoin, carbamazepine) increase the rate of metabolism of the oestrogen hormone and progestin, with consequent reduced contraceptive efficacy, and break-through bleeding during a cycle of pill administration. In a prospective study, patients with epilepsy on treatment with these drugs reported the failure of oral contraceptives. While oestrogen is pro-convulsant and progesterone anticonvulsant, there is no clear evidence that taking an oral contraceptive pill will adversely affect seizure control.

7. What is the recommended treatment during pregnancy?

Both uncontrolled seizures and AED use during pregnancy may have adverse effects on embryonic or foetal development. Consequently, the goal of epilepsy treatment during pregnancy should be to provide effective seizure control while minimizing adverse effects of AED therapy, which include increased risk for teratogenicity. Repeated seizures during pregnancy are associated with risks to both the mother and foetus, and may often be related to inadequate AED use. The benefits of appropriate AED therapy usually outweigh the risks associated with such therapy.

8. How can seizures be controlled during pregnancy?

The effect of pregnancy on seizure risk appears to vary among patients, but a sizeable percentage (17 per cent to 37 per cent) experience an increase in seizure frequency. Causes may include hormonal changes as well as lowered plasma levels of AEDs due to pharmacokinetic changes associated with pregnancy or to drug noncompliance. In addition, AED absorption may be reduced in some patients due to pregnancy related vomiting. Pharmacokinetic changes that occur during pregnancy include increased volume of distribution, increased renal elimination, altered hepatic enzyme activity, and reduced plasma protein concentrations. The net effect for most AEDs is an increase in clearance and a decrease in plasma levels. Seizure control is important not only because of the inherent risks to the patient but also because of potential danger to the foetus. Later in the pregnancy a maternal seizure may result in a fall that either injures the foetus or precipitates a miscarriage or early labour. However, up to 50 per cent of women report that their epilepsy is better controlled during pregnancy due to avoidance of excessive fatigue, and better drug compliance.

While simple partial, complex partial, absence and myoclonic seizures have not been found to adversely affect pregnancy or foetus, tonic clonic seizures carry the potential risk of miscarriage

due to impaired oxygenation. The best approach to seizure management in women planning to become pregnant is to establish effective control before conception. For most women and particularly those wishing to become pregnant, optimal treatment should include AED monotherapy. AED monotherapy has been associated with a lower risk for teratogenicity than has AED polytherapy. For example, counselling before pregnancy should include a discussion of pre-conception and gestational folate supplementation as prevention against malformations of the neural tube. Some AEDs can interfere with the absorption and metabolism of folate, which is required to support normal foetal development. Defects in neural tube closure can occur before a woman is likely to know that she is pregnant. Folic acid supplements—1 to 5 mg is recommended for women taking AEDs.

Infants exposed to hepatic CYP450 enzyme inducing AEDs in utero are at risk for vitamin K deficiency that can result in coagulopathy and neonatal intra-parenchymal and intracerebral haemorrhage during the first 24-hours of life. It is therefore recommended that pregnant women with epilepsy taking AEDs should receive vitamin K 10 mg/day by mouth during the last month of pregnancy. If the mother has not received vitamin K during the last month of pregnancy, it should be administered as soon as possible after the onset of labour. In addition, the neonate should receive vitamin K 1 mg i.m. at birth.

Breast Feeding: There are no contraindications to breastfeeding for women with epilepsy. In general, the benefits of breastfeeding for both infant and mother are believed to outweigh the small risk for adverse events associated with AED. Concentrations of AEDs in breast milk are generally low and not harmful to infants. Breast milk/maternal plasma fraction is 10 per cent for phenytoin, 5 per cent for valproate, 45 per cent for carbamazepine and 40 per cent for phenobarbital. However adverse effects such as sedation and

poor feeding may be specifically seen with exposure to barbiturates and benzodiazepines.

Role of Folic Acid: Serum folate concentration of less than 4 mcg/ml has been associated with an increased risk of foetal abnormalities. However 4mg/day folic acid given to women from preconception to early pregnancy has been shown to have a protective role.

Recommended Practice: Preconception counselling for the patient with respect to the risk of teratogenicity and possible adverse effects of uncontrolled seizures to maternal health is recommended. A thorough review of anti-epileptic drugs: aim for minimal effective monotherapy if epilepsy is active; consider drug withdrawal if the patient is seizure free.

Screen for malformation: At 16 weeks, elevated maternal levels of alphafeto-protein occur in 80 per cent of pregnancies, with neural tube defect. High resolution ultrasound may also detect neural tube defect at 16-18 weeks.

9. What if the patient is elderly?

The treatment of older adults poses a number of issues. Older individuals have a lower threshhold for development of side-effects, such as sedation, cognitive dysfunction, tremor and gait disturbance. Renal function is reduced. Therefore lower doses will be required for drugs that have renal clearance. Many common conditions in the elderly are treated with drugs that interact with commonly used AEDs. Any drug should be initiated at the lowest possible dose and titrate slowly to doses lower than those required in a younger patient. It is important not to make pre-existing problems worse by poor choice of drugs. Phenytoin is not a good choice for those with poor balance, likewise valproate is not

recommended for those with tremors or those taking sedatives for insomnia or patients with dementia.

Withdrawing Treatment

Discuss continuing or withdrawing AED treatment with adults who have been seizure free for at least three years. The discussion should include the risk of seizure reoccurrence while off-treatment and take account of his lifestyle and occupation. Drugs should be withdrawn gradually over a period of three months or longer; longer for benzodiapines (6 months or more); be aware of drug-related withdrawal symptoms or seizure recurrence. If on polytherapy, withdraw one drug at a time.

Educating the Patient and Family

A satisfactory relationship between the patient and physician is necessary for optimal management of epilepsy. This generally entails the patient and his/her family being actively involved in management decisions. Understanding the nature of the condition and how to deal with the challenges of living with an epileptic individual is important. Patients and their relations need to be aware of the nature of their seizures, and the precipitating factors and situations that should be avoided, the role of medications and need for their regular administration. The family needs practical advice about first aid procedures during a seizure. Issues relating to contraception, pregnancy and heredity should be discussed.

Normal Activities

Normal leisure activities should go on without undue restriction. Patients can join in normal social activities but they should avoid drinking too much alcohol. They should avoid situations which lead to sleep deprivation.

Safety at Home

Most accidents occur within the home. Often they result from careless errors or oversight.

Cooking

The kitchen can be a dangerous place for someone with frequent seizures. Gas or electric cookers should be handled with care. In the rural areas, the use of firewood and kerosene stoves should also be used with caution.

Bathing

The possibility of an epileptic patient having a seizure and drowning in a bath cannot be ruled out. Ideally, bathing should be done with a bucket or in a shower.

Sleeping

The risk of falling out of bed and injuring oneself can be minimized by sleeping on a mattress on the floor or a low level divan.

Driving

As a basic principle most people agree that individuals at high risk for losing consciousness or motor control should be prohibited from driving. Different countries have different regulations on these and several papers have been written on the subject. A commission of the International League Against Epilepsy has issued a comprehensive report on epilepsy and driving.

ILAE Recommendations on Driving

1. A driver's license should not be granted to individuals suffering from frequent seizures. A license may be granted if there is a prescribed period of freedom from seizures. The typical duration is 1-2 years.

2. Special circumstance should be considered, such as seizures only during sleep, seizure with prolonged and consistent auras or seizures precipitated by non-recurring circumstances.
3. An EEG is essential in the assessment for fitness to drive, but must be considered in the context of the whole clinical picture and not as a single determinant.
4. Persons who suffer from recurrent seizures should not drive.
5. Driving is not advisable while anticonvulsants are being withdrawn and for a period of three months thereafter.
6. After a single unprovoked seizure with negative subsequent investigation, the ban on driving should be reasonably short, for example 3-12 months.
7. Driver's license should not be withheld if seizures resulted from an acute cerebral illness which is not likely re-occur.
8. Seizures secondary to metabolic disorders should be evaluated on the basis of the underlying illness and how easily it can be controlled.
9. Driving may be permitted if seizures are provoked only by sensory stimuli such as photic stimulation, by avoiding of the precipitators.
10. Certain circumstances are high-risk for the emergence of epilepsy, for example brain abscess or certain types of cerebral trauma. Driving privileges should be withheld for some months after such insults. Individuals who have had seizures should be evaluated by a neurologist on an individual basis.
11. Medical advisory boards should be available to the licensing authorities to consider individual medical issues. Medical reassessment at appropriate intervals is recommended. Commercial driving regulations should generally be stricter

than those required for non commercial drivers, since the average time at the wheel and the consequences of an accident are higher for commercial drivers.

12. Physicians should be permitted, but not required to report individuals with epilepsy to the motor vehicle licensing authority. Required reporting encourages lack of honesty on the part of the patient, contributing in a counterproductive manner to poor seizure control.

Drug Treatment of Epilepsy in sub-Saharan Africa and Challenges

About 90 per cent of persons with epilepsy inhabit the developing world. Recent studies in developed and developing countries have shown that up to 70 per cent of newly diagnosed children and adults with epilepsy can be successfully treated with antiepileptic drugs; however, around 85 per cent may not receive any treatment at all. As a consequence, they experience morbidity related to seizures and the psychosocial consequences of stigma and discrimination.

Most of these people— many of whom are children—could have their seizures completely controlled and return to a normal life by taking a single daily dose of a drug. There are wide treatment gaps in these regions that need to be narrowed. Regrettably, patients with intractable epilepsy and seizures that could have otherwise been prevented continue to suffer endlessly in need of medication, facilities for epilepsy surgery, and education about the disease.

Delivery of Epilepsy Care in Nigeria[58]

Primary Care and Epilepsy

The primary health care service of the national health system is provided by the local governments. These include primary health care clinics and health centres.

Services at the village health centres and district health centre are provided by community health officers, supervisors and community extension workers. The national mental health policy calls for the integration of mental health into the national primary health care programme.

The term "mental health" is used in this context to include the care of major psychosis, epilepsy, mental retardation and dementia. Mental health has been incorporated into the ninth component of primary health care, and the standing orders on mental health for community workers have been developed. The orders for the junior community health extension workers at the village level require that cases of epilepsy be referred to the health centre. This means that there are no AEDs on the official drug list for the village dispensary.

The supervisors and assistants working at the district health centre can only treat acute seizures with paraldehyde or diazepam; suspected cases of epilepsy are referred to the general hospital.

General Medical Practitioners

Individuals and private groups own over one-third of health establishments in Nigeria. These are for profit health facilities, most often staffed by a single medical doctor in solo practice. Some private hospitals have more than one doctor. Private Hospitals are mostly concentrated in urban areas with very few in rural areas.

Most cases of epilepsy in urban areas are probably diagnosed and treated by general practitioners in private practice.

Secondary Health Care and Epilepsy

State Governments are responsible for secondary healthcare. The state general hospitals serve as referral centres for the district health centres. They have general out-patient departments run by general practitioners and are expected to have full complement of curative care with specialists in medicine, surgery, paediatrics and O&G. This is often not attained especially in most rural general hospitals. There is a full range of AEDs in the Essential Drugs List for secondary care levels. Of these, phenobarbital and phenytoin are more readily affordable; carbamazepine and valproate are too expensive for the majority of patients. There are no facilities for EEG and patients requiring EEG are referred to tertiary hospitals. An increasing number of well–equipped private hospitals in the urban centres provide a full complement of secondary health care services. EEG services are also available in some private hospitals in urban centres

Tertiary Health Care and Epilepsy

There are many teaching and neuropsychiatric hospitals providing tertiary care for patients in Nigeria. Most routine AEDs are available in tertiary care centres, but the high cost of certain drugs like valproate and scarcity of ethosuximide limit their usage..

None of the newer AEDs are available. The majority of epileptic patients in tertiary centres are seen as out-patients. Admissions for epilepsy are uncommon. There are no special centres for epilepsy in Nigeria. The development of efficient tertiary care in Nigeria is hampered by the inadequacy of specialists in clinical neurosciences and poor funding. The introduction of effective national health insurance plans may

eventually provide the funds for standard tertiary epilepsy care service in Nigeria.

The Epilepsy Treatment Gap in sub-Saharan Africa

A consensual definition of the "treatment gap" (TP) was adopted by international experts gathered together by the ILAE:

> The difference between the number of people with active epilepsy and the number whose seizures are being appropriately treated in a given population at a given point in time, expressed as a percentage.[59]

The reported size of the epilepsy TG in sub-Saharan Africa varies widely. A 2003 study estimated a TG of 70.3 per cent in the rural Kilifi district of Kenya, based on the absence of anti-epileptic drugs in blood samples of people with active convulsive epilepsy.[60] In Togo, the TG in six primary care centers, determined by treatment interruption, ranged from 94 per cent to 98 per cent in 2008.[61] Larger national and regional surveys are needed to more accurately determine the size and variability of the epilepsy TG within and between countries.

Leading causes of treatment gap include:

- Inadequate supplies and the prohibitive cost of anti-epileptic medications
- Lack of primary health workers trained to diagnose and treat epilepsy
- Limited access to health facilities particularly in rural areas;
- Social stigma, misinformation, and traditional beliefs
- Limited opportunities for specialty training in neurology

Ensuring adequate training of the health workers who provide the first level of contact in case detection, initiation of treatment with antiepileptic drugs, follow-up, and monitoring for compliance and adverse effects may be the most cost-effective ways to decrease the treatment gaps in the majority of countries.

Both cultural and structural factors affect the treatment gap. Cultural values affect people's health-seeking strategies. If people see epilepsy as caused by something that is not natural or biomedical, then treatment through Western medicine may not be sought. In many developing countries, epilepsy is perceived as a manifestation of supernatural forces. Usually the family and the patient first consult the traditional healers and follow their recommendations for a long period of time. The mean duration before seeking modern medical care can be several years.

Specialist care for epilepsy is usually unavailable at the community level and patients frequently need to travel long distances for proper diagnosis and treatment. Difficulty in travelling to obtain care was the main reason given for defaulting on follow-up at a rural epilepsy clinic in Ethiopia.[62] The mean duration for round-trip travel to the health centre was greater than ten hours. In most countries, phenobarbital is the only anti-epileptic medication in widespread use. Other standard drugs for epilepsy, including phenytoin, carbamazepine, and valproic acid, are commonly available but are significantly more costly. [63]

Unfortunately, inconsistent access to anti-epileptic drugs is cited by the ILAE as "both a cause of the treatment gap and the single most important obstacle to bridging the gap".[59] In a recent analysis of drug availability, surveys conducted in forty developing countries, including twelve countries in sub-Saharan Africa, phenobarbital and/or phenytoin was available in only 40.3 per cent and 29.4 per cent of facilities in the private and public sectors, respectively.[64] Despite its low cost, some patients in the poorest countries may still find the drug unaffordable. Compliance is a

frequent problem, since patients do not always appreciate the importance of taking daily medication for an intermittent condition. Medication toxicity and adverse interactions with other drugs are additional concerns. Unreliable supplies of medication, especially at rural clinics and dispensaries, make it difficult for many patients to maintain therapeutic blood levels. Finally, substandard and counterfeit medications are a growing concern which mainly affects developing countries.[65,66] Inadequate skilled manpower was the largest contributor to the epilepsy TG in developing countries according to the review by Mbuba, et al. [67] The median number of neurologists in sub-Saharan Africa is estimated at 0.3 per 1 million population, with eleven countries having none.[68] Another eleven countries have more than ten neurologists per country. These statistics are in sharp contrast to Europe where there are 48.4 neurologists per 1 million population.[69] Postgraduate neurology training programmes are only available in a few countries of sub-Saharan Africa.[69] The deficiency of neurologists translates into sparse neurological training of primary care physicians, clinical officers, nurses, and community health workers. Finally, the supply of diagnostic equipment to aid in the management of epilepsy (EEG machines, CT and MRI scanners) is extremely limited in many parts of Africa.[70]

The Use of Traditional Medicine and Spiritual Healing by Epileptic Patients in Nigeria[71]

Traditional Medicine

In contrast to developed countries where alternative medicine is at the fringe, Traditional medicine competes with or complements the Western type of medicine in African countries. Patients with epilepsy in Nigeria show a strong preference for traditional medicine over orthodox medicine especially in the rural areas.

Most of the herbal preparations are decoctions made by boiling different herbs in a pot of water and simmering them to allow the active ingredients to be extracted. Another preparation is a cold infusion using cow's urine. Several herbs, including onion bulbs, fresh tobacco leaves, and cow's urine are diluted in corn-steep liquor. The cow's urine serves as a source of ammonia, which, with the corn-steeped liquor assist in extracting the ether extractable alkaloids from the onion bulbs. Many children who ingest cow's urine preparations develop brain damage. According the study by Oyebola and Elegbe,[72] the toxicity is not due to the cow's urine but from nicotine poisoning from the extracts of the tobacco leaves

Spiritual healing

Epilepsy is often regarded as a manifestation of visitation by the devil, the effect of witchcraft or the revenge of an aggrieved ancestral spirit. Therefore, the management of epilepsy is commonly assumed to be in the domain of spiritual healers who hold out the attractive promise of a complete cure of the epilepsy by magical/spiritual therapies. These elaborate therapies include ritual dance, incantations, exorcism etc.

They often require considerable time, effort and money but are of considerable psychotherapeutic value in view of the deep rooted belief about the supernatural aetiology of epilepsy.

In a study by Danesi et al, of 265 patients who had used the above therapies before attending hospital, 47 per cent used traditional herbs, 20.4 per cent used spiritual healing.[71] However, only 14.6 per cent of those who had earlier used traditional herbs continued with the herbs, after commencing the more efficacious anti-epileptic drug treatment, but over two-thirds who had earlier used spiritual healing continued. This implies a strong perception of continuing psychological benefits from spiritual healing. However, many of such patients who discontinued anti-epileptic

drugs while in spiritual homes had increased seizure frequency with occasional status epilepticus. While not discouraged from seeking spiritual healing, epileptic patients are advised to continue taking their anti-epileptic drugs.

Epilepsy Surgery: Challenges for Sub-Saharan Africa

Epilepsy surgery for focal seizures began more than a century ago and have progressed with the technical innovations of EEG and neuroimaging. In the 1860s and 1870s, the pioneering clinical work of the epileptologist John Hughlings Jackson laid the groundwork for understanding the cortical localization of focal epilepsies, while the animal experiments of the neurophysiologists Gustav Theodor Fritsch, Eduard Hitzig, and David Ferrier gave parallel confirmation of Jackson's conclusions.

In 1886 Victor Horsley publicly presented his guidelines for antiseptic and hemostatic brain surgery in humans, focusing on three cases of young men subject to "fits." His lecture consisted of a detailed description of three epilepsy surgery cases. Jackson, on whose patient Horsley had operated, was in the audience and advised the conference attendees that surgery should be performed for seizures even in the absence of a mass lesion. Jackson's comments were paraphrased in the 1886 publication of Horsley's lecture: "Believing that the starting point of the fit was a sign to us of the seat of the 'discharging lesion,' he [Jackson] would advise cutting out that lesion, whether it was produced by tumour or not". Jackson was in fact recommending the resection of what was later to be called "the epileptogenic zone," regardless of the presence of structural abnormality.

Modern epilepsy surgery, dating back to the first operation undertaken by Sir Victor Horsley in London, UK, in 1886, is widely accepted as a cost-effective therapy for patients whose seizures are resistant to several antiepileptic drugs and who also have a

focal abnormality that can be removed. Although epilepsy surgery in resource-poor countries was first done in the 1950s, 80 per cent of developing countries are yet to have an epilepsy-surgery centre. There is an enormous gap between the number of patients who could benefit from epilepsy surgery and those who actually receive this treatment. Of the low-income countries, 4 per cent mention provision of surgery as a task of epilepsy specialists compared with 37.9 per cent of high-income countries. When people with epilepsy continue to have frequent seizures despite multiple-drug therapy, epilepsy surgery may be indicated. Surgery can provide a significant improvement in the quality of life for some of the 20 per cent to 30 per cent of people with epilepsy who continue to have seizures while taking appropriate medication.

Epilepsy surgery is not available in 87 per cent of low-income countries. Facilities for epilepsy surgery are also absent in 34.3 per cent of high-income countries.

Patients with potentially epileptogenic, well-circumscribed lesions on MRI and patients with mesial temporal lobe epilepsy are reasonable candidates for surgery. Palliative epilepsy surgeries include corpus callosotomy and other disconnections. These operations are feasible in developing countries with a knowledgeable team consisting of an epileptologist, neurosurgeon, and technicians and with using MRI and EEG, as basic investigative technologies.

Whereas the treatment gap for epilepsy is of considerable concern in the developing world, there is a marked treatment gap with respect to epilepsy surgery even in industrialized countries, where perhaps only 5 per cent of potential surgical candidates are ever referred to an epilepsy surgery centre. Until recently, epilepsy surgery was not available in countries with limited resources, but epilepsy surgery programmes are now prominent in Brazil, China, India, and Turkey and are being developed in many other countries with limited resources, where it is recognized as a more

cost-effective treatment for surgically remediable syndromes than continued pharmacotherapy.

The success of epilepsy surgery depends upon the accurate identification of good surgical candidates, and then selecting the best candidates based on the available resources and technologies without jeopardizing their safety. It also depends on a well-trained clinical team, including a neurologist, neurosurgeon, clinical neurophysiologist, neuropsychologist, neuroradiologist, and psychiatrist, more so than on high-level diagnostic and surgical technology.

Neurologists and neurosurgeons in China are also in the process of advising the government to establish a multi-tiered system for epilepsy surgery. However, China is still in the early phase of implementing surgical treatment and offers only a few hundred conventional epilepsy surgery procedures a year—with most cases being adult temporal lobectomy.

In Latin America, which has a population of half a billion, the situation is variable, says Américo Sakamoto, a neurologist at the University of São Paulo in Brazil and chair of the Latin American Epilepsy Surgery Subcommittee of the International League Against Epilepsy (ILAE). In the past few years, the subcommittee has been assessing the situation in Latin America to determine the necessary steps to implement epilepsy surgery more broadly and to narrow the surgical treatment gap. Its study shows that epilepsy surgery is done to high standards in some countries, such as Brazil, Mexico, Argentina, and Chile, but similar treatment is either basic or non-existent in others, such as Paraguay, Bolivia, Peru, and countries in Central America.

Not all developing countries, however, are suitable for implementing epilepsy-surgery facilities, notes Gretchen Birbeck, director of the Epilepsy Care Team at Chikankata Hospital in Mazabuka, Zambia. In some African countries, where even basic

anti-epileptic drugs are not available, surgical interventions might be a step too far. In most countries in sub-Saharan Africa, the treatment gap for any disease, including epilepsy, is about 90 per cent—which is a result of a combination of factors such as inadequate public health systems, unreliable drug purchasing, and scarcity of properly trained medical staff. "Until we can manage first-line treatment for epilepsy, there is be no point in implementing epilepsy surger," she says.

This situation in sub-Saharan Africa cannot remain static. Although the average number of trained neurologists in sub-Saharan Africa is less than 0.3 per 1 million population, some countries have more neurologists than others. Countries such as South Africa and Nigeria now have a modest number of neurologist and neurosurgeons. MRI and other investigations are becoming available. Epilepsy surgery may be feasible in these countries in the not so distant future.

Even in developing countries where epilepsy surgery is feasible and accessible, there are problems of affordability. Brazil is one of the few countries that includes the procedures, costing between $5000—$10,000, as part of the public health system. Patients elsewhere would have to bear the cost on their own. A straightforward temporal lobectomy costs about $1500 in India and $8500 in China, which is beyond the reach of many people in those countries.

Vagus Nerve Stimulation[73]

Vagus nerve stimulation (VNS) received approval for use in USA in 1997, as an adjunct therapy of medically intractable epilepsy in adults and in adolescents older than 12 years. The VNS delivers chronic intermittent current to the left vagus nerve based on programmed parameters which are adjusted for seizure control and tolerability. In addition to the baseline stimulation, patients

are instructed in the use of a magnet to trigger the stimulation to abort a seizure. Clinical VNS trials have demonstrated seizure reduction and improvement in quality-of-life measures. Significant side-effects which appear to improve over time include hoarseness, cough and shortness of breath.

The vagus nerve carries the somatic and visceral afferent and efferent fibres. Efferent fibres travel widely throughout the body, innervating the pharynx and larynx, heart, and abdominal viscera. The presumed targets of VNS are the afferent fibres, originating largely from the parasympathetic ganglia near the base of the skull and brainstem. These afferents synapse in the medullary nuclei. The nucleus of tractus solitarius (NTS) is the medullary structure most densely innervated by the synapsing vagal afferents. The NTS also receives projections from a very wide range of sources, including peripheral nerves, the spinal cord, brain stem, structures and hypothalamic regions. In turn, the NTS projects extensively to multiple brain stem and subcortical regions, with significant noradrenergic and serotonergic innervation. While the exact mechanism remains unclear, NTS is likely significantly involved in the anti-seizure properties of VNS.

Long term studies suggest that the efficacy of VNS therapy will increase over time, while side effects such as dyspnoea tend to decrease over time. VNS therapy is associated with improvement in the quality of life measures in both responders and non-responders.

Vagal nerve stimulation for intractable seizure is not yet available in sub-Saharan Africa, but may be available in future for a selected group of patients who can afford it. The constraint is the inadequate number of trained personnel who can implant and maintain it.

Recommendations to Address Epilepsy management Challenges in Sub-Saharan Africa

Prevention of Epilepsy in Sub-Saharan Africa

Multidisciplinary efforts focusing on the risk factors (eg, enforcement of strict traffic regulations to prevent trauma) or providing specific protection (eg, immunization against communicable diseases) for these preventable causes can help to substantially decrease incidences of epilepsy.

The role of individuals in preventing epilepsy should include the prevention of road traffic accidents by careful driving, prompt treatment of fever to prevent febrile convulsions in children, immunization of children to prevent infectious diseases that can cause epilepsy as a long term sequelae.

The role of the primary health care service should be to provide maternal and child care to prevent birth injuries from obstructed labour, immunizations to prevent childhood infections and prompt treatment of febrile illness and febrile seizures. The role of secondary and tertiary health care service in the prevention of epilepsy is prompt treatment of CNS infections such as meningitis and other bacteria and parasitic infections of the nervous system.

Integration of Epilepsy Prevention in Public Health Interventions

As many cases of epilepsy in developing countries arise from other health problems, the epilepsy programme should be included in primary health care national plans and coordinated with other public health programmes that take place at government and community level. In particular, the plans directed towards mother and child, pregnant women and first decade paediatric health, should take into consideration that complications in the peri-

partum period are the leading causes of future epilepsy in developing countries. Major measures for primary prevention should include improving awareness and taking action on:

1. Increasing and improving prenatal consultation and medically assisted delivery
2. Improving maternal and infant immunization
3. Prevention and better management of work and road accidents by making the wearing of helmets obligatory
4. Avoiding alcoholic and environmental toxicology
5. Highlighting, managing and preventing infectious diseases that affect the brain
6. Preventing consanguine marriages

Intervention to Close the Treatment Gap

Based on the discussion above, a multitude of interventions are necessary to reduce the epilepsy treatment gap in sub-Saharan Africa. At the international level, increased advocacy for epilepsy is necessary to raise awareness of this condition as a major non-communicable disease.

The Global Campaign Against Epilepsy was started in 1997 to bring epilepsy "out of the shadows".[74] Increasing the supply of health workers capable of diagnosing and treating epilepsy is a critical need.

The small numbers of physicians trained in neurology in many countries represents an obvious deficiency that can only be remedied by additional post-graduate training programmes, partnership with neurology training programs in developed countries, and incentives to retain neurologists and reduce the 'brain drain'.

The majority of people with epilepsy in sub-Saharan Africa will need medical treatment by primary health care providers at

the community level. Therefore, neurologists will need to engage in organized educational programmes to train primary care physicians, clinical officers, nurses, and community health workers, so they can carry out the basic services required to manage epilepsy. This task-shifting can only be accomplished if government health ministers, regional and national neurological associations, and funding agencies work synergistically to disseminate neurological knowledge to lower cadres of health workers. Primary health care providers should be trained to administer validated screening surveys and perform simple neurological exams in their communities to identify residents with possible epilepsy. A neurologist (or physician specializing in epilepsy) can review all positive screening results to confirm a diagnosis of epilepsy. The neurologist may be located at a secondary or tertiary hospital or may visit the rural clinic on a regular schedule. The neurologist can facilitate any required diagnostic testing (EEG, CT, MRI, lab tests) and recommend appropriate anti-epileptic drugs.

The primary provider is then responsible for managing the patient's condition by:

1. Tracking seizure frequency (using patient-maintained seizure calendar)
2. Monitoring medication compliance and side effects
3. Ordering laboratory tests and drug levels
4. Providing education and social support

A community-based intervention trial using a similar protocol was successfully implemented in rural China.[75]

The following measures can be taken:

1. Setting up a training programme on epilepsy for general MDs and medical specialists, nurses and midwives, social workers and school teachers;
2. Developing or adapting existing guidelines for epilepsy management;
3. Strengthening the capacity of medical schools in the region to train specialists in the fields of neurology, neurosurgery and psychiatry and increase the time devoted to epilepsy in current curricula.

Drug Supply

A reliable procurement and distribution of anti-epileptic medications at low cost are critical. The lack of a regular and reliable drug supply is reported as a major problem in three-quarters of low-income countries.[76] Although phenobarbital has a number of significant drawbacks as a first-line medication for epilepsy,[77] it is probably the only drug with reasonable potential for widespread scale-up and acceptance, since out-of-pocket expenses are the main source of healthcare financing in most of sub-Saharan Africa.[76]

Human Resource Development

Post-graduate training in neurology should be concentrated and supported at established medical schools in selected countries. Some neurologists would need to be sponsored for epilepsy fellowship training in Europe or the United States.

Most importantly, working conditions, salaries, and benefits would have to be attractive enough to prevent newly trained neurologists from emigrating to wealthier countries seeking highly skilled professionals.[78] Concurrent with the training of more

neurologists, educational activities will need to be developed and supported to teach primary health care workers basic skills in diagnosing and managing epilepsy. These programmes will require partnerships between government agencies, non-government organizations, and professional societies.

The World Federation of Neurology and the WHO have already made commitments to support educational initiatives for physicians and non-physicians.[79] Much of this training will depend on volunteerism by neurologists from developed countries. The distribution of evidence-based and easy-to-follow manuals to evaluate and treat seizure disorders, such as the WHO mhGAP intervention guide,[80] will help facilitate the process of task-shifting to non-specialist health providers.

Educating the Public

Various groups, ie, decision-makers, professionals, people with epilepsy and their families, teachers, and primary health care workers, police and the general public, have to be targeted. The community should be given adequate information to reduce stigma related to the condition. Epilepsy is not contagious, epilepsy is treatable, and people with epilepsy can enjoy better lives and become valuable members of the community. Training of health care workers is essential if people with epilepsy are to be correctly diagnosed and appropriately treated. Improving local competence at primary and secondary health care levels is a necessity.

Culturally Appropriate Information

Closing the gap in epilepsy care will require the dissemination of culturally appropriate information about seizures and the importance of proper medical treatment. In many communities, people with epilepsy are not seeking appropriate treatment

because of social isolation, superstition, and/or reliance on traditional healers. Increasing patient knowledge through community-based education programmes can enhance medication compliance, improve seizure outcomes, and reduce stigma.[81]

The Cultural Environment

Serious consideration of the cultural environment is needed to effectively reduce the treatment gap. Information and education of the public in general is important in order to enable and empower people to make informed choices. Cultural aspects should be studied with regard to patients' perceptions, attitudes and practices in relation to epilepsy, as well as their socio-familial relations. This information which is essential in designing an appropriate treatment programme has a greater chance of success if adapted in a holistic way to cultural specificities. Furthermore research should be done to find out how apparent conflicts between cultural and scientific concepts can be resolved.

Collaboration with Traditional Healers and Community Leaders

Because the majority of patients will have consulted traditional healers, a noncompetitive relationship should be encouraged. Sharing information and research and offering training to traditional healers would strengthen this collaboration.

Field experience has shown that working closely with traditional healers, community and religious leaders would give the primary health care worker a better opportunity to gain acceptance from the community and modify certain harmful practices.

Conclusion

The future of epilepsy treatment in sub-Saharan Africa will remain challenging given the many barriers discussed above. Continued advocacy for people with epilepsy will require more epidemiologic research to document the true burden of disease and magnitude of the treatment gap in different countries. In the short term, improving the availability of phenobarbital and other generic first-line anti-epileptic drugs should be given the highest priority. The more difficult challenge will be to increase the number of skilled health care workers capable of diagnosing and treating epilepsy. International neurological organizations, including the International League Against Epilepsy, the International Brain Research Organization, the World Federation of Neurology, and the American Academy of Neurology, should increase their efforts to develop and support epilepsy training curricula and programmes in sub-Saharan Africa.

In the last decade, the disproportionate majority of global health funding has been allocated to vertical programs targeting HIV/AIDS, malaria, and tuberculosis.[82] The renewed calls for action to raise the priority of chronic non-communicable diseases in global health planning and research are encouraging.[83] Funding commitments from domestic governments, international donors, non government organizations, industry, and private philanthropists will be critical to scaling up access to anti-epileptic medications and building capacity in human resources for epilepsy care in sub-Saharan Africa. It has been suggested that a global fund for epilepsy should be established to accelerate donor support and coordinate programme development and implementation, both in sub-Saharan Africa and in other resource-limited regions of the world.

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