



National Epilepsy Consensus

Guideline of Bangladesh



SOCIETY OF NEUROLOGISTS OF BANGLADESH

Scientific Partner



SANOFI

"Sanofi Bangladesh Limited is a subsidiary
of Beximco Pharmaceutical Limited"

National Epilepsy Consensus Guideline Bangladesh



Society of Neurologists of Bangladesh

First Edition: 2021

Scientific Partner



"Sanofi Bangladesh Limited is a subsidiary
of Beximco Pharmaceutical Limited"

Advisory Board

- Prof. Anisul Hoque
- Prof. Quazi Deen Mohammad
- Prof. Dr. AKM Anwar Ullah
- Prof. Firoz Ahmed Quraishi
- Prof. Abu Nasir Rizvi
- Prof. Mohammad Mizanur Rahman
- Prof. M A Hannan
- Prof. Md. Rezaul Karim Khan
- Prof. Md. Rafiqul Islam
- Prof. Md. Badrul Alam
- Prof. Sakhawat Hossain
- Prof. Hasan Zahidur Rahman
- Prof. Md. Motiur Rahman
- Prof. Md. Azharul Hoque
- Prof. Mansur Habib
- Prof. Shaheen Akhter
- Prof. Md. Ashraf Ali
- Prof. Maliha Hakim
- Prof. Narayan Saha
- Prof. Kafil Uddin
- Prof. Akhlaque Hossain Khan
- Prof. Kanuj Kumar Barman
- Dr. Narayan Chandra Kundu
- Prof. Zahed Ali
- Prof. Md. Hassanuzzaman
- Dr. Swapon Kumar Ghose
- Prof. Rajib Nayan Chowdhury
- Dr. SK Mahabub Alam
- Dr. Abu Saleh Md. Badrul Hasan
- Dr. Mohammad Enayet Hussain
- Dr. Ahmed Ashafuddoula
- Dr. Abdus Salam

Editorial Board

- Prof. Firoz Ahmed Quraishi
- Prof. Abu Nasir Rizvi
- Prof. Md. Rafiqul Islam
- Prof. Maliha Hakim
- Prof. Narayan Saha
- Prof. Kanuj Kumar Barman
- Dr. Swapon Kumar Ghose
- Prof. Rajib Nayan Chowdhury
- Dr. SK Mahabub Alam
- Dr. Mohammad Enayet Hussain
- Dr. A F M Al Masum Khan

Head of Editorial Board

Prof. Dr. Md Rafiqul Islam

Ex Chairman and Professor
Department of Neurology
BSMMU

Acknowledgement

Guideline has long been recognized as a useful adjunct to clinical based and continuing professional development. It emphasize the need for clinical reasoning, integrating thinking, problem solving, communication, teamwork and self-directed learning – all desirable generic skills for health care professionals. Epilepsy is amongst the most frequently encountered of neurological disorders. There are important emerging clinical issues (e.g. first seizure, therapy-resistant seizures, ICU, pregnancy, pediatric) but also differential diagnosis of non-epileptic seizures (syncope, pseudo-seizure, paroxysmal dystonic syndromes, sleep disorders, psychosis etc.). This selection of epilepsy will inform clinicians at all stages in their career. Including both common and uncommon scenarios, National Epilepsy Consensus Guideline of Bangladesh reinforces the diagnostic skills and treatment decision-making processes necessary to treat epilepsy and other seizures confidently. Written by leading experts in neurologists from Bangladesh, the cases and discussions work through differential diagnoses, treatments and social consequences in pediatric and adult patients.

The editors collected protocols, treatment regimen, drug selection and real life experiences from International guidelines. For this purpose, chapters were selected to illustrate common and more rare conditions of patients.

The collection of these topics will add clinical experiences to more systematic and theoretical-based textbooks of epilepsies providing a systematic overview.

General and special remarks guide the reader through the special requirements of the case and refer to systematic information by recommended publications.

Assemble of chapters of guideline will always pose a challenge for its editors. In the guideline we have heavily edited some individual contributions and worked assiduously in conjunction. Every effort has been made in the preparation and editing of guideline to ensure that the details given will educate and make more informative in epilepsy treatment. I wish to express our gratitude to all the editors and all the contributors to 1st edition of National Epilepsy Consensus Guideline of Bangladesh.

Prof. Dr. Md. Rafiqul Islam

Former Chairman, Dept. of Neurology, BSMMU

Head of Editorial Board, National Epilepsy Consensus Guideline of Bangladesh

Preface

Globally around 50 million people live with epilepsy, where the overall prevalence of epilepsy in Bangladesh is 8.4 per 1000. But the matter of sorrow is that most of the patients with epilepsy remain untreated due to some clinical, social, and economic impacts. Around 80% of people with epilepsy (PWE) live in the 'developing', low- and middle-income, or resource-poor countries in tropical or subtropical regions.

Most developed countries adopted evidence-based national guidelines at minimum of a decade ago, with these regularly being updated to improve epilepsy-care services. Etiologies of epilepsy, the expertise of the healthcare personnel, diagnostic capacity, treatment options, and cultural perception of the disorder differs from low-income and high-income regions. The etiology of epilepsy in Bangladesh varies with that in developed countries being birth trauma, birth asphyxia, central nervous system infections are common causes in neonate and infancy whereas head trauma,

brain tumor, stroke, infections are common causes in middle aged and elderly.

Considering these the Society of Neurologists of Bangladesh (SNB) has decided to publish a set of guidelines for the management of epilepsy in the country which would be helpful to General practitioners, Internists, Paediatricians, Psychiatrists, Neurologists and all relevant health care providers. With this aim a core committee and an epilepsy working committee comprising of Neurologists and Paediatric Neurologists were formed. The recommendations in the guidelines are based on recent publications as well as the expert opinions of the panel.

Epilepsy is a common neurological disorder, but the treatment of epilepsy is not straightforward. In low-income countries like Bangladesh, about three quarters of people with epilepsy may not receive the treatment they need. Individual clinician's skill, knowledge and attitude, drug selection

strategy like starting, switching and stopping capability, drug toxicity and interaction alert, compliance and follow up, patient and caregiver's awareness, social reaction to epilepsy-all these factors may play a crucial role in the management of epilepsy. This Clinical Practice Guidelines are introduced to improve the treatment management and rational use of AEDs which could be a helpful resource for HCPs updating.

Heartfelt gratitude goes to all members and working committee of the SNB who have worked for more than a year-long to bring the vision into daylight. We express thanks to the core-committee of SNB for their efforts and guidance all through its journey.



Prof. Firoz Ahmed Quraishi

President

Society of Neurologists of
Bangladesh



Prof. Abu Nasir Rizvi

General Secretary

Society of Neurologists of
Bangladesh

Table of content

1.0 Introduction	19-20
1.1 Key facts	20
2.0 Definition	22-22
2.1 Conceptual definition of seizure and epilepsy (ILAE 2005 report)	22
2.2 Practical clinical definition	22
2.3 Diagnosis of an epilepsy syndrome	22
2.4 Active epilepsy	22
3.0 Classification	24-29
ILAE classification of seizure types basic version	24
ILAE classification of seizure types expanded version	25
3.1 International classification of seizures (1981)	25
3.1.1 Partial seizures (start in one place)	25
3.1.2 Generalized seizures (apparent start over wide areas of brain)	25-26
3.1.3 Unclassifiable seizures	26
3.2 Classification of epilepsies and epileptic syndromes	26
3.3 International classification of epilepsies and Epileptic syndromes	26-27
3.4 Idiopathic epilepsies	27
3.4.1 Idiopathic focal epilepsies/ Idiopathic Localization-related epilepsy	26
3.4.2 Idiopathic generalised epilepsies	26-27

3.5 Symptomatic epilepsies	28
3.5.1 Symptomatic focal epilepsies	28
3.5.2 Symptomatic generalized epilepsies	28
3.6 Cryptogenic epilepsies	28
3.6.1 Cryptogenic focal epilepsies	28
3.6.2 Cryptogenic generalized epilepsies	28-29

4.0 Epilepsy differentials **31-33**

4.1 Overview	31
4.2 Syncope	31
4.2.1 Vasovagal syncope	31
4.2.2 Cardiac syncope	31
4.2.3 Reflex anoxic syncope	31
4.2.4 Breath-holding attacks	31
4.2.5 Hyperventilation syncope	31
4.2.6 Compulsive valsalva	31
4.2.7 Neurological syncope	31
4.2.8 Imposed upper airways obstruction	31
4.2.9 Orthostatic intolerance	31
4.2.10 Long QT and cardiac syncope	31
4.3 Vascular	31
4.3.1 TIA	31
4.4 Behavioral, psychological and psychiatric disorders	31
4.4.1 Daydreaming / Inattention	31
4.4.2 Self-gratification	31
4.4.3 Tantrums and rage reactions	31
4.4.4 Out of body experiences	31
4.4.5 Panic attacks	31
4.4.6 Dissociative states	31

4.4.7 Non-epileptic seizures	31
4.4.8 Hallucinations in psychiatric disorders	31
4.4.9 Fabricated / factitious illness	31
4.5 Sleep related conditions	31
4.5.1 Sleep related rhythmic movement disorders	31
4.5.2 Hypnagogic jerks	31
4.5.3 Parasomnias	31
4.5.4 REM sleep disorders	31
4.5.5 Benign neonatal sleep myoclonus	31
4.5.6 Periodic leg movements	31
4.5.7 Narcolepsy-cataplexy	31
4.6 Paroxysmal Movement Disorders	31
4.6.1 Tics	31
4.6.2 Stereotypies	31
4.6.3 Paroxysmal kinesigenic dyskinesia	31
4.6.4 Paroxysmal nonkinesigenic dyskinesia	31
4.6.5 Paroxysmal exercise induced dyskinesia	31
4.6.6 Benign paroxysmal tonic upgaze	32
4.6.7 Episodic ataxias	32
4.6.8 Alternating hemiplegia	32
4.6.9 Hyperekplexia	32
4.6.10 Opsoclonus-myoclonus syndrome	321
4.7 Migraine associated disorders	32
4.7.1 Migraine with visual aura	32
4.7.2 Familial hemiplegic migraine	32
4.7.3 Benign paroxysmal torticollis	32
4.7.4 Benign paroxysmal vertigo	32
4.7.5 Cyclical vomiting	32
4.8 Miscellaneous events	32

4.8.1 Benign myoclonus of infancy and shuddering attacks	32
4.8.2 Jitteriness	32
4.8.3 Gastro-oesophageal reflux Sandifer Syndrome	32
4.8.4 Non-epileptic head drops	32
4.8.5 Raised intracranial pressure	32
4.8.6 Paroxysmal extreme pain disorder	32
4.8.7 Spinal myoclonus	32
4.8.8 TGA (Transient Global Amnesia)	32
4.9 Common differential of epilepsy according to age	32
4.10 Transient loss of consciousness	33

5.0 Brief description of important clinical conditions 35-38

5.1 Syncope	35
5.2 Vasovagal Syncope	35
5.3 Cardiac Syncope	35
5.4 Vascular	35
5.4.1 TIA	35
5.5 Behavioral, psychological & psychiatric disorders	36
5.5.1 Rage reactions	36
5.5.2 Panic attacks	36
5.5.3 Non-epileptic seizures (NEAD)	36
5.6 Sleep related conditions	36
5.6.1 Parasomnias	36
5.6.2 Benign neonatal sleep myoclonus	36
5.6.3 Narcolepsy-cataplexy	37
5.7 Paroxymal movement disorders	37
5.7.1 Tics	37

5.8	Migraine associated disorders	37
5.8.1	Migraine with visual aura	37
5.9	Miscellaneous events	37
5.9.1	Benign myoclonus of infancy and shuddering attacks	37
5.9.2	Jitteriness	37
5.10	TGA (Transient Global Amnesia)	38
6.0	Differentiating points between three most common Causes of episodic loss of consciousness	40-41
7.0	Investigations	43-43
7.1	Overview	43
7.1.1	The main objectives of investigating patients with epilepsy	43
7.2	Types of investigation	43
7.2.1	EEG	43
7.2.2	Neuroimaging	43
7.2.3	Other investigation- blood tests, muscle biopsy	43
7.2.4	Neuropsychological assessment	43
8.0	Electroencephalogram (EEG)	45-45
9.0	Neuroimaging	47-47
10.0	Other tests	49-49
11.0	Neuropsychological assessment	51-51
12.0	General information about pharmacological treatment	53-54
12.1	Pharmacological management	53
12.1.1	Steps of general management	53
12.1.2	Patients need counseling	53

12.1.3 Life style modification	53
12.2 Pharmacological treatment of epilepsy	53
13.0 How to start anti- epileptic drug treatment	56-56
13.1 Approach to long term pharmacological treatment of epilepsy	56
14.0 When & how to stop anti-epieptic drug treatment	58-58
15.0 Recommended AED according to seizure type or Epilepsy syndrome	60-63
15.1 Recommended drugs for Bangladesh by SNB	63
16.0 Dosing frequency	65-74
16.1 Modes of action of AEDs	68-69
16.2 AEDs pharmacokinetics & adverse reactions	70-73
16.3 Key messages and special recommendations for specific drugs	73-74
17.0 Surgical treatment of epilepsy	76-77
17.1 Definition of epilepsy surgery	76
17.2 Indication of epilepsy surgery	76
17.3 Contra-indication of epilepsy surgery	76
17.3.1 Absolute	76
17.3.2 Relative	76
17.4 Refractory epilepsy	76
17.4.1 Definition	76
17.4.2 Criteria	76
17.4.3 Factors considered in the decision making process for Refractoriness	76-77
17.4.4 Factors associated with resistance to AED therapy	77
18.0 Comprehensive epilepsy care program	79-79

18.1 Functions of comprehensive epilepsy care program	79
18.2 Types of surgical procedures of intractable epilepsy	79
18.2.1 Resective operations	79
18.2.2 Functional operations	79
19.0 Emergency management of epilepsy	81-82
19.1 Initial supportive management for compulsive seizure	81
19.2 Get patient to the nearest hospital	81
19.3 Emergency AED therapy needed	81-82
20.0 Treatment for prolonged seizure	84-85
20.1 Prolonged seizures & acute repetitive seizure	84
20.1.1 Alternative to parenteral benzodiazepines	85
20.1.2 Treatment algorithms for convulsive status epilepticus	85
20.1.3 Management during post status phase	85
21.0 Epilepsy in special situations	87-94
21.1 Epilepsy in women	87
21.2 Epilepsy & menstruation	87
21.3 Fertility & epilepsy	88
21.4 Contraception	88
21.5 Pre-conception management & counseling	89
21.6 Monitoring during pregnancy for mother & fetus	90
21.7 Management during labour	91
21.8 Lactation	91-92
21.9 Driving & epilepsy	93

21.10 Eclampsia & other hypertensive conditions	93
21.11 Anticoagulation	93
21.12 AEDs in hepatic disease	93
21.13 AEDs in renal disease	94
21.14 Obesity & AEDs	94
21.15 Epilepsy in elderly	94

22.0 Management of pediatric epilepsy

96-112

22.1 Epileptic encephalopathy	96
22.2 Epileptic syndrome	96-97
22.3 Epileptic syndrome: neonatal onset	98-99
22.4 Infantile spasm	99-101
22.5 Treatment with Intramuscular Acth	102
22.6 Treatment with oral Prednisolone UKISS protocol	102
22.7 Treatment with oral Vigabatrin	102
22.8 Severe Myclonic Epilepsy of infancy/ Dravet Syndrome	103
22.9 Natural course of Dravet Syndrome	104-106
22.10 Epielpsy with Myclonic Atonic Seizure (Doose Syndrome)	106-107
22.11 Lennox - Gastaut Syndrome (LGS)	107
22.12 Difference among common childhood epileptic syndromes	108
22.13 Landau-Kleffner syndrome (LKS)	108
22.14 Treatment	109
22.15 Genetic epilepsy with febrile seizure plus– GEFS+	109
22.16 Self-limited epilepsies of childhood	109

22.17 Panayiotopoulos syndrome	109-110
22.18 Clinical & EEG features of main self-limited Childhood epilepsies	110-111
22.19 Childhood absence	111
22.20 Childhood absence: ILAE criteria	111
22.21 Febrile seizure	112
22.22 Defined by ILAE	112
22.23 National Institute of Health Consensus	112
22.24 Classification of febrile seizure	112
23.0 Conclusion	114-114
24.0 Disclaimer	116-116
References	118-125

1.0 Introduction

19-20

1.1 Key facts

20

1.0 Introduction

The word “epilepsy” is derived from the Greek “epilepsia” which means “to take hold of” or “to seize.”

Hippocrates view of epilepsy as a brain disorder began to take root in the 18th and 19th centuries. The intervening 2000 years were dominated by the earlier supernatural views. Throughout this time, people with epilepsy were viewed with fear, suspicion and misunderstanding and were subjected to enormous social stigma. They were treated as outcasts and punished. However, some of them succeeded and in fact became famous all over the world. Among them were Julius Caesar, Czar Peter the great of Russia, Pope Pius IX, The writer Fyodor Dostoevsky, The poet Lord Byron and others. Even today, people with epilepsy continue to suffer discrimination in the family, marriage, employment, law, education and society.

An estimation of 50 million people worldwide live with epilepsy ^[1,2] most of whom remain untreated ^[3]. The overall prevalence of epilepsy in Bangladesh per 1000 is 8.4 ^[4]. The etiology of epilepsy in Bangladesh varies with that in developed countries being birth trauma, birth asphyxia, central nervous system infections are common causes in neonate and infancy whereas head trauma, brain tumor, stroke, infections are common causes in middle aged and elderly ^[5].

To improve epilepsy-care services, most developed countries adopted national guidelines

at least a decade ago, with these being regularly updated ^[6-8]. Such guidelines, wherever possible, are evidence-based, relying upon the body of evidence for best care practices in high-income, resource-rich countries with predominantly moderate climates. However, 80% of people with epilepsy (PWE) live in the so-called ‘developing’, low-income, or resource-poor countries in tropical or subtropical regions. Low-income and high-income regions differ substantially in terms of the underlying etiologies of epilepsy, the expertise of the healthcare personnel, diagnostic capacity, treatment options, and cultural perception of the disorder. Guidelines for use in the resource-poor environments must address factors specific for the clinical and sociocultural setting. Valid guidelines are of paramount importance for low-income tropical regions as the mortality and morbidity associated with epilepsy in such regions may be relatively high even when there is available treatment, and the treatment gap remains vast, with less than 20% of people with active epilepsy in most developing countries receiving treatment^[9]. Adopting healthcare guidelines prepared for higher-resourced areas and using these in resource-limited settings is neither appropriate nor feasible for many reasons including resource restrictions ^[10]. Considering all these issues Society of Neurologists Bangladesh (SNB) has decided to publish a set of guideline for the management of epilepsy in the country which would be helpful to

General practitioners, Internists, Paediatricians, Psychiatrists, Neurologists and all relevant health care providers. With this aim a core committee and an epilepsy working committee comprising of Neurologists and Paediatric Neurologists were formed. The recommendations in the guidelines are based on recent publications as well as the expert opinions of the panel.

1.1 Key facts: ^[11]

Epilepsy is a chronic non-communicable disease of the brain that affects people of all ages. Worldwide more than 50 million people have epilepsy, making it one of the most common neurological diseases globally.

Nearly 80% of people with epilepsy live in low and middle income countries.

It is estimated that 70% of people living with epilepsy could live seizure free if properly diagnosed and treated.

About three quarters of people with epilepsy living in low and middle income countries do not get the treatment they need.

In many parts of the world, people with epilepsy and their families suffer from stigma and discrimination. Prevalence in Bangladesh is 8.4/1000.

2.0 Definition

22-22

2.1	Conceptual definition of seizure and epilepsy (ILAE 2005 report)	22
2.2	Practical clinical definition	22
2.3	Diagnosis of an epilepsy syndrome	22
2.4	Active epilepsy	22

2.0 Definition

2.1 Conceptual Definition of Seizure and Epilepsy (ILAE 2005 report)

An epileptic seizure is a transient occurrence of signs and/or symptoms due to abnormal excessive or hyper synchronous neuronal activity in the brain.

Epilepsy is a disorder of the brain characterized by an enduring predisposition to generate epileptic seizures, and by the neurobiologic, cognitive, psychological, and social consequences of this condition. The definition of epilepsy requires the occurrence of at least one epileptic seizure. So, a seizure is an event and epilepsy is the disease involving recurrent unprovoked seizures.

Acute symptomatic seizures (Syn: provoked seizure/reactive seizure) provoked by metabolic or toxic derangements or occurring acutely in the setting of head trauma or stroke do not define epilepsy.

2.2 Practical Clinical Definition:^[12]

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

- At least two unprovoked (or reflex) seizures occurring >24 h apart

- One unprovoked (or reflex) seizure and a probability of further seizures similar to the general recurrence risk (at least 60%) after two unprovoked seizures, occurring over the next 10 years

2.3 Diagnosis of an Epilepsy Syndrome

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

2.4 Active Epilepsy

A prevalent case of active epilepsy is defined as a person with epilepsy who has had at least one epileptic seizure in the previous five years, regardless of anti-epileptic drug treatment.

3.0 Classification

24-29

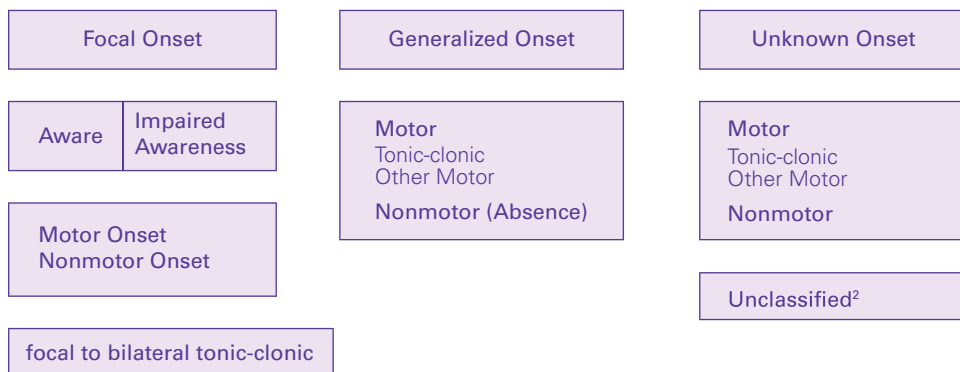
ILAE classification of seizure types basic version	24
ILAE classification of seizure types expanded version	25
3.1 International classification of seizures (1981)	25
3.2 Classification of epilepsies and epileptic syndromes	26
3.3 International classification of epilepsies and Epileptic syndromes	26
3.4 Idiopathic epilepsies	27
3.5 Symptomatic epilepsies	28
3.6 Cryptogenic epilepsies	28

3.0 Classification

Epileptic seizures are classified on the basis of their clinical features alone (Table 1) whereas the classification of epilepsies and epileptic syndromes is based on electro clinical criteria described by the International Classification of Epilepsies and Epileptic syndromes. The latter

also provides information about the possible aetiology, anatomical basis, precipitating factors, age of onset, severity, chronicity, diurnal and circadian cycling, and sometimes prognosis of the epilepsies.

ILAE 2017 Classification of Seizure Types Basic Version



¹Definitions, other seizure types and descriptors are listed in the accompanying paper & glossary of terms

²Due to inadequate information or inability to place in other categories^[13]

ILAE 2017 Classification of Seizure Types Expanded Version

Focal Onset		Generalized Onset	Unknown Onset
Aware	Impaired Awareness	Motor Tonic-clonic clonic tonic myoclonic myoclonic-tonic-clonic myoclonic-atic tonic epileptic spasms	Motor Tonic-clonic epileptic spasms Nonmotor behavior arrest
Motor Onset automatisms atonic ² clonic epileptic spasms ² hyperkinetic myoclonic tonic Nonmotor Onset autonomic behavior arrest cognitive emotional sensory		Nonmotor (Absence) typical atypical myoclonic eyelid myoclonia	Unclassified ²
focal to bilateral tonic-clonic			

¹ Definitions, other seizure types and descriptors are listed in the accompanying paper and glossary Of terms

²These could be focal or generalized, with or without alteration of awareness

³ Due to inadequate information or inability to place in other categories [13]

3.1 International Classification of Seizures (1981)

3.1.1 Partial Seizures (start in one place)

Simple (no loss of consciousness or memory)

- Sensory
- Motor
- Sensory-Motor
- Psychic (abnormal thoughts or perceptions)

- Autonomic (heat, nausea, flushing, etc.)

Complex (consciousness or memory impaired)

- With or without aura (warning)
 - With or without automatism
- Secondarily generalized

3.1.2 Generalized Seizures (apparent start over wide areas of brain)

- Absence (petit mal)
- Tonic-clonic (grand mal)

- Atonic (drop seizures)
- Myoclonic
- Other

3.1.3 Unclassifiable Seizures ^[14]

Consciousness is maintained in simple partial seizures but impaired in complex partial seizures. The symptomatology of partial seizures (seizure semiology) reflects the anatomical origin of the seizures. Hence, partial seizures may be characterized by motor, special sensory, autonomic or psychic symptoms. In addition, complex partial seizures are typically accompanied by automatisms; consisting of involuntary movements, e.g. lip smacking, chewing, fidgeting and wandering.

3.2 Classification of Epilepsies and Epileptic Syndromes:

Epilepsy classification is undertaken after the criteria for diagnosing epilepsy are met (definition above). Classification is undertaken using a multi-level classification framework, involving classification at three levels - the seizure type, epilepsy type and epilepsy syndrome. Imaging, EEG and other investigations, where available, contribute to optimized classification at all three levels. Where possible, a diagnosis at all three levels should be established. The etiology of the epilepsy should be considered from the outset, and at each step along the diagnostic pathway. Knowing the etiology can inform optimized classification and has important treatment implications for the patient.

3.3 International Classification of Epilepsies and Epileptic Syndromes^[15]

1.0 Localization-related (focal, local, partial) Epilepsies and Syndromes

1.1 Idiopathic (with age-related onset)

- Benign childhood epilepsy with Centro temporal spikes
- Childhood epilepsy with occipital paroxysms
- Primary reading epilepsy

1.2 Symptomatic

1.2.1 Characterized by simple partial seizures*

1.2.2 Characterized by complex partial seizures*

1.2.3 Characterized by secondarily generalized seizures*

1.3 Unknown as to whether the syndrome is idiopathic or symptomatic

2.0 Generalized Epilepsies and Syndromes

2.1 Idiopathic

- Benign familial neonatal convulsions
- Benign neonatal convulsions
- Benign myoclonic epilepsy in infancy
- Childhood absence epilepsy (pyknolepsy)
- Juvenile absence epilepsy
- Juvenile myoclonic epilepsy
- Epilepsy with generalized tonic-clonic seizures on awakening

*With the characteristics of seizures arising from frontal, parietal, temporal, Occipital, or multiple lobes; or the locus of onset is unknown.

2.2 Cryptogenic or Symptomatic

- West syndrome
- Lennox-Gastaut syndrome
- Epilepsy with myoclonic-astatic seizures
- Epilepsy with myoclonic absences

2.3 Symptomatic

2.3.1 Non-specific aetiology

- Early myoclonic encephalopathy

2.3.2 Specific syndromes

- Epileptic seizures complicating disease states

3.0 Epilepsies and Syndromes Undetermined, Whether Focal or Generalized

3.1 With both generalized and focal seizures

- Neonatal seizures
- Severe myoclonic epilepsy in infancy
- Epilepsy with continuous spike and wave EEG during slow-wave sleep (CSWS)
- Acquired epileptic aphasia (Landau-Kleffner syndrome)

3.2 Without unequivocal generalized or focal features

4.0 Special Syndromes

4.1 Situation-related seizures

- Febrile convulsions
- Isolated seizures or isolated status epilepticus
- Seizures occurring only when there is an acute metabolic or toxic event

Based on ILAE syndromic classification of epileptic syndromes, epilepsy can be divided into “idiopathic”, “symptomatic” and “cryptogenic”.

Idiopathic epilepsies are genetically determined and have no structural cause, no associated clinical signs, normal brain imaging and normal EEG background.

Symptomatic epilepsies have known causes and cryptogenic epilepsies have an underlying cause that cannot be documented objectively. Thus, cryptogenic epilepsies are more likely to be symptomatic than idiopathic.

3.4 Idiopathic Epilepsies

3.4.1 Idiopathic focal epilepsies/ idiopathic localization-related epilepsy

The two common types of benign focal epilepsy of childhood are those with centrotemporal spikes (BCECTS) and those with occipital paroxysms. This list is not exhaustive as newer syndromes have been described since the 1989 ILAE classification, for example Autosomal dominant nocturnal frontal lobe epilepsy (ADNFLE).

3.4.2 Idiopathic Generalised Epilepsies

These syndromes are genetically determined, and patients have a normal neurological examination and normal intelligence. The EEG shows generalised epileptiform discharges and may show photosensitivity.

Childhood absence epilepsy, previously known as petit-mal epilepsy, is characterized by an age of onset between 4 and 10 years, typical absences, generalized tonic-clonic seizures (GTCS) in about 50% of patients, myoclonic seizures in a minority of patients, and generalised 3Hz spike-wave activity on EEG. Other examples include

juvenile absence epilepsy that occurs at a later age.

Patients with juvenile myoclonic epilepsy (JME) tend to be older (onset in adolescence), and have myoclonic jerks usually in the morning on awakening with or without GTCS, generalized bilateral symmetrical polyspikes and generalized spike-wave complexes on their EEG, and rarely, go into remission.

3.5 Symptomatic Epilepsies

3.5.1 Symptomatic Focal Epilepsies

Seizures arise from a localized region of the brain. If the cause is found, these epilepsies are symptomatic. The common causes are hippocampal sclerosis, low-grade tumours (DNET, ganglioglioma) and cortical dysgenesis.

Mesial temporal lobe epilepsy, most commonly caused by hippocampal sclerosis in adults and cortical dysgenesis and low-grade tumours Dysembrioplastic neuroepileptical tumour (DNET) in children, is characterized by epigastric phenomena (abdominal), psychic auras and complex partial seizures with orofacial and manual automatisms with or without secondary generalization.

The causes of temporal, occipital, frontal and parietal neocortical epilepsy are more diverse, and include traumatic scars, neoplasms, vascular malformations, infarcts, haemorrhages and cortical malformations. Seizure semiology, consisting of simple partial or complex partial seizures, depends upon the area of neocortex affected.

3.5.2 Symptomatic Generalized Epilepsies

These epilepsies are associated with diffuse brain dysfunction. Common causes include previous anoxic birth injury, underlying metabolic derangement or chromosomal defect. There is usually clinical evidence of intellectual deficiency and/or developmental delay. The clinical and EEG findings are usually abnormal and age-dependent.

3.6 Cryptogenic Epilepsies

3.6.1 Cryptogenic focal epilepsies

The underlying cause for the focal seizure cannot be found.

3.6.2 Cryptogenic generalized epilepsies

The underlying cause for the generalized seizure cannot be found.

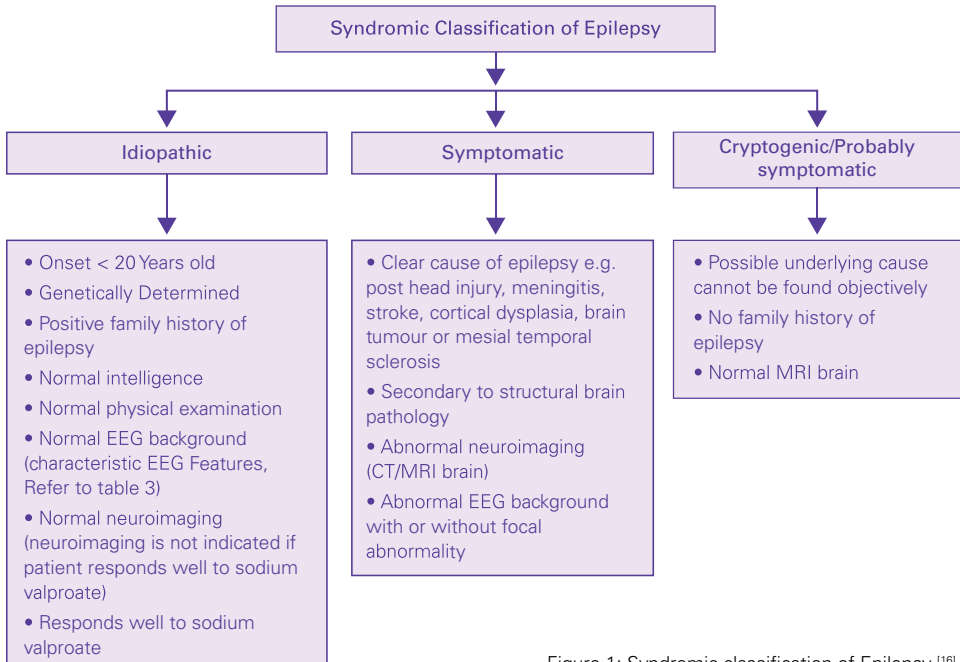


Figure 1: Syndromic classification of Epilepsy ^[16]

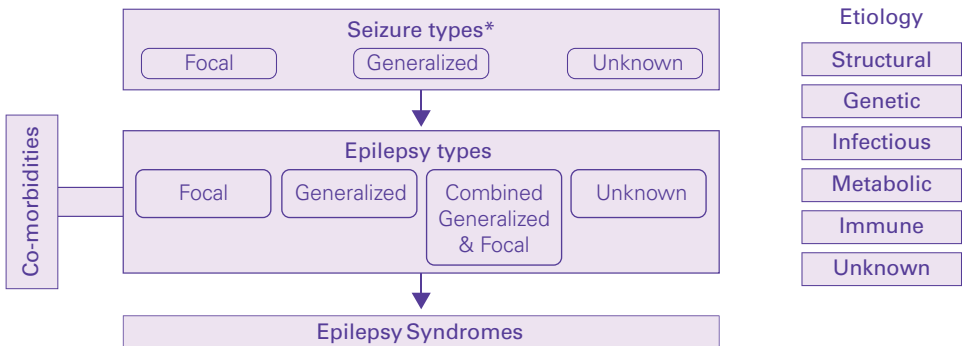


Figure 2: Framework for classification of the epilepsies.

*Denotes onset of seizure. Epilepsia ILAE

4.0 Epilepsy differentials

31-33

4.1	Overview	31
4.2	Syncope	31
4.3	Vascular	31
4.4	Behavioral, psychological and psychiatric disorders	31
4.5	Sleep related conditions	31
4.6	Paroxysmal Movement Disorders	31
4.7	Migraine associated disorders	32
4.8	Miscellaneous events	32
4.9	Common differential of epilepsy according to age	32
4.10	Transient loss of consciousness	33

4.0 Epilepsy differentials

4.1 Overview

There are different conditions associated with recurrent paroxysmal events that may mimic and be misdiagnosed as epilepsies. It is important that these disorders are considered in the evaluation of paroxysmal events. History remains the key to a correct diagnosis with video recordings are helpful. History should be taken from the patient, parents or witness of the event. There are some conditions in which epileptic and non-epileptic events may co-exist. Epilepsy mimics vary with age. Following are few examples of mimics of epilepsy ^[17]

4.2 Syncope

- 4.2.1 Vasovagal syncope
- 4.2.2 Cardiac syncope
- 4.2.3 Reflex anoxic syncope
- 4.2.4 Breath-holding attacks
- 4.2.5 Hyperventilation syncope
- 4.2.6 Compulsive valsalva
- 4.2.7 Neurological syncope
- 4.2.8 Imposed upper airways obstruction
- 4.2.9 Orthostatic intolerance
- 4.2.10 Long QT and cardiac syncope

4.3 Vascular ^[18]

- 4.3.1 TIA

4.4 Behavioral, Psychological and Psychiatric Disorders

- 4.4.1 Daydreaming /inattention
- 4.4.2 Self-gratification
- 4.4.3 Tantrums and rage reactions
- 4.4.4 Out of body experiences
- 4.4.5 Panic attacks
- 4.4.6 Dissociative states
- 4.4.7 Non-epileptic seizures
- 4.4.8 Hallucinations in psychiatric disorders
- 4.4.9 Fabricated / factitious illness

4.5 Sleep Related Conditions

- 4.5.1 Sleep related rhythmic movement disorders
- 4.5.2 Hypnagogic jerks
- 4.5.3 Parasomnias
- 4.5.4 REM sleep disorders
- 4.5.5 Benign neonatal sleep myoclonus
- 4.5.6 Periodic leg movements
- 4.5.7 Narcolepsy-cataplexy

4.6 Paroxysmal Movement Disorders

- 4.6.1 Tics
- 4.6.2 Stereotypies
- 4.6.3 Paroxysmal kinesigenic dyskinesia
- 4.6.4 Paroxysmal nonkinesigenic dyskinesia
- 4.6.5 Paroxysmal exercise induced dyskinesia

- 4.6.6 Benign paroxysmal tonic upgaze
- 4.6.7 Episodic ataxias
- 4.6.8 Alternating hemiplegia
- 4.6.9 Hyperekplexia
- 4.6.10 Opsoclonus-myoclonus syndrome

4.7 Migraine Associated Disorders

- 4.7.1 Migraine with aura
- 4.7.2 Familial hemiplegic migraine
- 4.7.3 Benign paroxysmal torticollis
- 4.7.4 Benign paroxysmal vertigo
- 4.7.5 Cyclical vomiting

4.8 Miscellaneous Events

- 4.8.1 Benign myoclonus of infancy and shuddering attacks
- 4.8.2 Jitteriness
- 4.8.3 Gastro-oesophageal reflux (Sandifer syndrome)
- 4.8.4 Non-epileptic head drops
- 4.8.5 Raised intracranial pressure
- 4.8.6 Paroxysmal extreme pain disorder
- 4.8.7 Spinal myoclonus
- 4.8.8 TGA (Transient Global Amnesia)

4.9 Common Differentials of Epilepsy According to Age^[19]

Adults

- Syncope
- Migraine
- Transient global amnesia
- Transient ischaemic attacks
- Paroxysmal movement disorders and ataxias

Young children

- Breath holding spells
- Reflex anoxic syncope
- Parasomnias
- Benign paroxysmal vertigo
- Tics
- Rage attacks

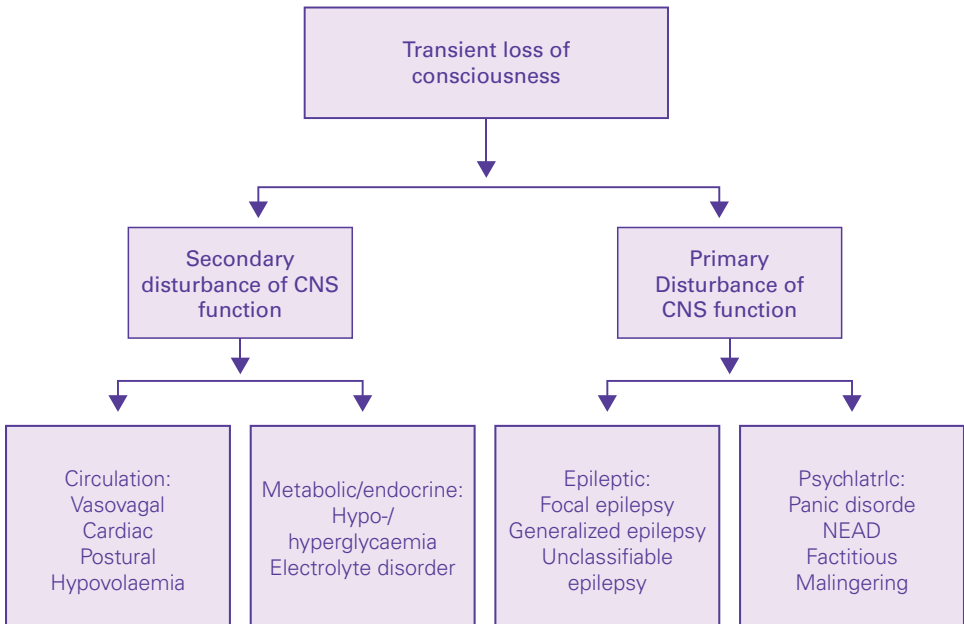
Neonate and infants

- Jitteriness and benign myoclonus
- Gastro-oesophageal reflux
- Hyperekplexia

Any age

- Metabolic & endocrine causes
- Drug induced dystonia
- Cardiac dysrhythmias
- Non-epileptic attack disorder (NEAD)

4.10 A simple approach to differentiate between common causes of transient loss of consciousness^[20]



5.0 Brief description of important clinical conditions

35-38

5.1	Syncope	35
5.2	Vasovagal Syncope	35
5.3	Cardiac Syncope	35
5.4	Vascular	35
5.5	Behavioral, psychological & psychiatric disorders	36
5.6	Sleep related conditions	36
5.7	Paroxymal movement disorders	36
5.8	Migraine associated disorders	36
5.9	Miscellaneous events	36
5.10	TGA (Transient Global Amnesia)	38

5.0 Brief description of important clinical conditions

5.1 Syncope

Syncope (fainting) describes the transient loss of consciousness. Syncope occurs when there is an abrupt reduction in blood flow and oxygen supply to the brain. Vasovagal & cardiac syncope's are common.

5.2 Vasovagal syncope

Vasovagal syncope affects all ages. Prolonged standing, dehydration, change in posture and emotional upset are the important triggers for syncope. The syncope occurs in particular situation, for example hair brushing, venipuncture in a doctor's surgery or standing up in a place of worship is important.

There is reduced blood pressure and slowing of the heart rate causing lack of blood flow to the brain. Early symptoms include blurring and loss of vision, ringing in the ears and dizziness. Associated pallor and autonomic symptoms such as sweating, flushing, feeling warm, nausea and abdominal discomfort may co-exist. The fall in a vasovagal syncope is usually flaccid.

These are brief, lasting for seconds, and can be distinguished from tonic seizures and generalized tonic-clonic seizures due to the shorter duration, presence of triggers, associated symptoms and quick recovery. The tonic-clonic movements are typically not rhythmic.

Following syncope there may be brief period

of confusion. Injury can occur in syncope, as can tongue biting (this is often at the tip of the tongue; whereas lateral tongue biting suggests a tonic-clonic seizure). Urinary incontinence may also be present in syncope.

Interictal EEG is not of any diagnostic or prognostic value for syncope. Tilt table testing, which may trigger syncope, may have some value in special situations.

5.3 Cardiac syncope

Both tachyarrhythmia and bradyarrhythmia can produce syncope. There may be prodromal features of palpitation, chest pain, shortness of breath or other features of cardiovascular insufficiency. These attacks do not have relation with posture, position or specific triggers.

5.4 Vascular

5.4.1 TIA

Transient ischemic attack is defined as episode of focal cerebral, retinal, or spinal cord ischemia causing transient neurologic dysfunction lasting <24 h (most TIAs resolve in <1 h). Despite complete symptom resolution 20%-50% with TIA have evidence of acute tissue infarction on MRI. AHA revised definition: TIA should only refer to transient episode of neurologic dysfunction due to ischemia without evidence of acute infarction, regardless symptom duration.

Symptoms of TIA are impaired speech and or language, Visual loss in one or both eyes, double vision, facial drooping, swallowing dysfunction, unilateral weakness, unilateral sensory loss, impaired limb coordination, vertigo, and gait dysfunction. TIA/stroke is differentiated from seizure by abrupt onset; fixed focal findings refer to arterial distribution and DW-MRI may be abnormal in 20%-50% with transient symptoms.

5.5 Behavioral, Psychological and Psychiatric Disorders

5.5.1 Rage reactions

Rage reactions, episodic dyscontrol or intermittent explosive disorders are characterized by situations in which there are recurrent episodes of rage which seem to be out of proportion to relatively minor stimuli. Sustained outbursts of aggression may occur for many minutes, sometimes for up to half an hour or longer.

5.5.2 Panic attacks

Panic or anxiety attacks are brief episodes, each lasting several minutes, which can recur. A sudden feeling of apprehension, fear or terror is accompanied by symptoms including breathlessness (with hyperventilation), choking sensation, palpitations, chest pain, paraesthesia (typically perioral and in the hands), dizziness, sweating, trembling and feeling faint or loss of consciousness.

5.5.3 Non-epileptic seizures (NEAD)

Non-epileptic attack disorders (previously known as non-epileptic attacks, psychogenic seizures

and pseudoseizures) mimics epileptic seizures, but does not have any electrophysiological correlation. Psychogenic factors play important role for the development of non-epileptic seizures.

The seizure-like event may include movement or impaired awareness, and can imitate focal motor seizures or focal impaired awareness seizures. Motor features that distinguish these attacks from seizures include a prominence of proximal or truncal movements, waxing and waning pattern of movements, variable rate and direction of jerking, horizontal movements of the head, crying during or after the event, and eye closure with resistance to passive eye opening.

Video EEG monitoring and concomitant psychological evaluation is typically required to establish the diagnosis and the treatment plan.

5.6 Sleep related conditions

5.6.1 Parasomnias

Arousal parasomnias including night terrors, sleep walking and confusional arousals are behaviors that arise out of deep non-REM sleep (stages 3 & 4), typically in the first third of the night's sleep. Arousal parasomnias are common and can be regarded as part of normal sleep unless the behavior produces disruption to the individual or their family.

5.6.2 Benign neonatal sleep myoclonus

Benign neonatal sleep myoclonus is a normal sleep phenomenon which can be very frequent in some infants leading to misdiagnosis as myoclonic seizures or generalized tonic-clonic seizures. The myoclonus only occurs in sleep

and the infants have a normal neurological examination, with normal feeding and behavior.

5.6.3 Narcolepsy-cataplexy

Narcolepsy-cataplexy is a sleep disorder, where person directly enters into REM. Onset is typically in the teenage years though it can occur later in life, having HLA association. Recurrent fall & sleep paralysis is common presentation of this disorder.

5.7 Paroxysmal movement disorders

5.7.1 Tics

Tics are characterized by sudden, rapid, repetitive, non-rhythmic, simple or complex involuntary movements or vocalizations. Simple motor tics involve a single muscle or group of muscles (including ocular muscles) and may be misdiagnosed as myoclonic seizures. Complex motor tics involve a cluster of simple actions or coordinated sequence of movements that may be purposeful or non-purposeful. Tics are common in childhood and have a tendency to wax and wane in frequency over time.

5.7.2 Hyperekplexia

Hyperekplexia is actually an exaggeration of the normal startle response, having genetic associations. Symptoms are evident from the neonatal period or early infancy. In response to normal touch, noise or any unexpected stimulus they can startle excessively with flexion of the limbs and retraction of the head.

5.8 Migraine associated disorders

5.8.1 Migraine with visual aura

Migraine with aura and its variants are very common and it is well established that migraine and epilepsy often co-exist as co-morbid disorders. The visual aura of migraine preceding a headache can take a variety of forms but is typically in one visual field and contains positive phenomena such as flashes, arcs of lights (fortification spectra), specks, or flames and negative phenomena such as scotoma with blanking out or greying of the visual field.

Visual phenomena of occipital seizures are more likely to be colored and can include a variety of different shapes including diamonds, squares, circles and lines. More complex sensory illusions or perceptions may be found that may or may not precede a headache.

5.9 Miscellaneous events

5.9.1 Benign myoclonus of infancy and shuddering attacks

Benign myoclonus of infancy and shuddering attacks are both benign (self-limiting) variants of normal behavior in infants. These attacks typically have onset from 4 months of age and can persist up to the age of 6-7 years, with a remitting and relapsing course. Attacks can be very frequent and can last a few seconds in duration. Certain activities such as feeding, head movements can trigger an attack.

5.9.2 Jitteriness

Jitteriness is common in the newborn period, commonly occurring in an otherwise well-

appearing infant on the first day of life as a transient, self-limiting finding. Medical causes of jitteriness may include hypocalcemia and neonatal abstinence syndrome. Jitteriness can be distinguished from epileptic seizures as it can be increased when the infant is unwrapped, stimulated, startled or crying, but suppresses when the infant is wrapped or the affected limb is held gently.

anterograde memory function lasting upto few hours, unable to record new memories, resulting in repetitive questioning. TGA is benign, self-limiting, no investigation or treatment is necessary

5.10 TGA (Transient Global Amnesia)^[18]

Features of Transient global amnesia are middle aged people with abrupt, discrete loss of

6.0 Differentiating points between three most common causes of episodic loss of consciousness

40-41

6.0 Differentiating points between three most common causes of episodic loss of consciousness

Semiological features for differentiating between the three most common causes of transient loss of consciousness

Observation	Generalized Tonic-Clonic Seizure	Syncope	Psychogenic non-epileptic seizures
Onset	Focal onset possible (aura duration typically <30 seconds)	Common (pre syncopal symptoms, duration often minutes)	Not infrequent (often lasting several minutes)
Motor activity	Typical seizure patterns (tonic, clonic, tonic-clonic)	Myoclonic jerks common (short duration, rapid recovery) after loss of postural tone	Commonly undulating motor activity with sudden pauses but stable frequency
Asynchronous arm and leg movements	Unusual	Not rare (multifocal myoclonus)	Common
Purposeful movements	Very rare	Rare	Occasional
Rhythmic pelvic movements	Rare	Never	Occasional
Opisthotonus, 'arc de cercle'	Very rare	Occasional ('decerebrate' posturing)	Occasional
Prolonged ictal atonia	Very rare	Not >60 seconds	Occasional
Skin	Cyanosis common	Pallor, sweating	No cyanosis despite long seizure duration
Ictal crying	Very rare	Very rare	Occasional

Observation	Generalized Tonic-Clonic Seizure	Syncope	Psychogenic non-epileptic seizures
Closed eyes	Rare	Rare	Very common
Resistance to eye opening	Very rare	Very rare	Common
Maintained pupillary light reflex	Often abolished	Common	Very common
Ictal reactivity	Rarely preserved	Rarely preserved	Occasionally partially preserved
Ictal incontinence	Not rare	Rare	Not rare
Seizure duration >2 minutes	Uncommon	Very uncommon (only if patient supported in upright posture)	Common
Postictal reorientation	Mostly over minutes	<1 minute (exception: head injury caused by collapse/ patient maintained in upright position)	Often unexpectedly quick or slow
Tongue biting	Not infrequent (lateral)	Occasional (tip)	Occasional (tip)
Injury	Common (burns)	Rare	Common
Seizures at night (from 'sleep')	Common	Rare	Not rare

Important Points of Chapter

- Differential diagnosis of epilepsy is widely variable.
- Certain disorders are prevalent in different age groups.
- It is important to differentiate between seizure and syncope.
- History from the patient and parents/ witness of the event is necessary for differentiation.
- Movement disorders, nocturnal events, NEAD and different pediatric non-epileptic disorders need to be excluded.
- Home video recording of the event with mobile phone is important for decision making.

7.0 Investigations

42-42

7.1	Overview	43
7.2	Types of investigation	43

7.0 Investigations

7.1 Overview

Proper counseling is required before doing the investigations. Diagnosis of epilepsy is mainly clinical. Investigations neither confirm nor refute a diagnosis. Diagnosis of epilepsy is incomplete without knowing its aetiology and prognosis. On the other hand, doctors might over investigate patients presenting with epileptic seizure. A rational approach is needed to avoid unnecessary investigations or not to omit essential investigations.

7.1.1 The main objectives of investigating patients with epilepsy are

- Clarify the diagnosis of epilepsy and non-epileptic attack.
- Determine the nature of the seizure types and epilepsy syndromes

- Localization of seizure onset
- Identify the etiology of epilepsy
- Look for concomitant problems
- Monitor the disease progression and consequence of treatment

7.2 Types of investigation

7.2.1 EEG

7.2.2 Neuroimaging

7.2.3 Other investigation- blood tests, muscle biopsy

7.2.4 Neuropsychological assessment

8.0 Electroencephalogram (EEG)^[21]

45-45

8.0 Electroencephalogram (EEG)^[21]

8.1 An EEG should be performed only to support a diagnosis of epilepsy in adults, children and young people in whom the clinical history suggests that the seizure is likely to be epileptic in origin.

8.2 If an EEG is considered necessary, it should be performed after the second epileptic seizure but may, in certain circumstances, as evaluated by the specialist, be considered after a first epileptic seizure.

8.3 An EEG may be used to help determine seizure type and epilepsy syndrome in children, young people and adults in whom epilepsy is suspected. This enables them to be given the correct prognosis.

8.4 In patients presenting with a first unprovoked seizure, unequivocal epileptiform activity shown on EEG can be used to assess the risk of seizure recurrence.

8.5 Repeated standard EEGs may be helpful when the diagnosis of the epilepsy or the syndrome is unclear. Once diagnosis of epilepsy is established repeat EEGs are not necessary.

8.6 When a standard EEG has not contributed to diagnosis or classification, a sleep EEG should be performed.

8.7 In children and young people, a sleep EEG is best achieved through sleep deprivation or the use of melatonin.

8.8 Long-term video or ambulatory EEG may be used in the assessment of children, young people and adults who present diagnostic difficulties after clinical assessment and standard EEG.

8.9 Provocation by suggestion may be used in the evaluation of non-epileptic attack disorder.

8.10 Photic stimulation and hyperventilation should remain part of standard EEG assessment. Patient or attendant should be informed that, these provocations might precipitate seizure.

8.11 An EEG should not be performed in the case of probable syncope because of the possibility of a false-positive result.

8.12 The EEG should not be used to exclude a diagnosis of epilepsy in a person in whom the clinical presentation supports a diagnosis of a nonepileptic event.

8.13 The EEG should not be used in isolation to make a diagnosis of epilepsy.

9.0 Neuroimaging^[21]

9.1 Neuroimaging should be used to identify structural abnormalities that cause certain epilepsies.

9.2 MRI of brain should be the imaging investigation of choice in patients with epilepsy.

9.3 MRI of brain is particularly important in those:

- Who develop epilepsy before the age of 2 years
- In adulthood- who have any suggestion of a focal onset on history, examination or EEG (unless clear evidence of benign focal epilepsy) in whom seizures continue in spite of first-line medication.

9.4 Neuroimaging should not be routinely requested when a diagnosis of idiopathic generalised epilepsy has been made.

9.5 CT head should be used to identify underlying gross pathology in cases

- If MRI is not available
- MRI is contraindicated
- Children or young people in whom a general anaesthetic or sedation would be required for MRI but not CT.
- In an acute situation, CT may be used to determine whether a seizure has been caused by an acute neurological lesion or illness.

10.0 Other tests^[21]

10.1 Measurement of serum prolactin is not recommended for the diagnosis of epilepsy.

10.2 In adults, appropriate blood tests (for example, plasma electrolytes, glucose, calcium) to identify potential causes and/or to identify any significant comorbidity should be considered

10.3 In children and young people, other investigations, including blood and urine biochemistry, should be undertaken at the direction of the specialist to exclude other diagnoses, and to determine an underlying cause of the epilepsy.

10.4 A 12-lead ECG should be performed in adults with suspected epilepsy.

10.5 In cases of diagnostic uncertainty, a referral to a cardiologist should be considered.

11.0 Neuropsychological assessment^[21]

51-51

11.0 Neuropsychological assessment^[21]

11.1 Referral for a neuropsychological assessment is indicated

- When a child, young person or adult with epilepsy is having educational or occupational difficulties
- When an MRI has identified abnormalities in cognitively important brain regions.
- When a patient complaint of memory or other cognitive deficits and/or cognitive decline.

Important points of chapter

- First unprovoked seizure is an indication for investigations.
- EEG is important for classifying epilepsy.
- MRI of brain is indicated for focal epilepsy.
- CT head can be done in acute situation.
- Blood tests, ECG can be done in selective cases
- Neuropsychological assessment is necessary in epileptic patients having learning & cognitive dysfunction.

12.0 General information about pharmacological treatment

53-54

12.1	Pharmacological management	53
12.2	Pharmacological treatment of epilepsy	53

12.0 General information about pharmacological treatment

12.1 Pharmacological Management^[22]

Once diagnosis is made patient and family members need to be counseled empathically. Since the disease still carries a strong stigma, confidentiality needs to be maintained at all steps, and the condition should be discussed with any family member with consent of the patient.

12.1.1 Steps of general management:

1. Establish the diagnosis
2. Education/counseling
3. Address psychosocial issues
4. Lifestyle modifications

12.1.2 Patients need counseling regarding the

- a. Disease
- b. Diagnosis
- c. Need for medication
- d. Compliance
- e. Life style

12.1.3 Life style modification includes

- Adequate sleep - early to bed early to rise
- Change in job e.g. occupation driving, swimmers, boxers, airplane pilots etc.
- Avoidance of alcohol, stimulants, energy drinks, chewing tobacco etc.
- Stress reduction - specific techniques, Yoga, meditation, early morning walks

- Adequate diet - high protein. Low carbohydrate, Vit. D, B rich diet
- Joining support groups
- Avoid social isolation

12.2 Pharmacological treatment of epilepsy^[23]

The mainstay of treatment for epilepsy is antiepileptic drugs (AEDs) taken daily to prevent the recurrence of epileptic seizures. It is important that the treatment strategy and suitability of the AED is determined by the physician keeping the individual with epilepsy and the care-givers informed before drug therapy is started.

- AED therapy should only be started once the diagnosis of epilepsy is confirmed, except in exceptional circumstances that require discussion and agreement between the physician and the child, young person or adult and their family and/or care-givers as appropriate.
- The decision to initiate AED therapy should be taken between the child, young person or adult, their family and/or care-givers (as appropriate) and the physician after a full discussion of the risks and benefits of treatment. This discussion should take into account details of the person's epilepsy syndrome, prognosis and lifestyle.

- Treatment with AED therapy is generally recommended after a second epileptic seizure.
- When possible, choose which AED to offer on the basis of the presenting epilepsy syndrome. If the epilepsy syndrome is not clear at presentation, base the decision on the presenting seizure type(s).
- AED therapy should be considered and discussed with children, young people and adults and their family and/or care-givers as appropriate after a first unprovoked seizure if:

- The child, young person or adult has a neurological deficit
- The EEG shows definite epileptic activity
- The child, young person or adult and/or their family and/or care-givers consider the risk of having a further seizure unacceptable
- Brain imaging shows a structural abnormality.

13.0 How to start anti- epileptic drug treatment

56-56

13.1 Approach to long term pharmacological treatment of epilepsy

56

13.0 How to start anti- epileptic drug treatment

13.0 How to start anti- epileptic drug treatment^[24]

Mono therapy with the appropriate AED is preferred. If uncontrolled, adjunctive AED is added, and sometimes even a third AED is required for resistant cases.

Selection of AED is highly individualized. Considerations while choosing an AED include:

- I. Efficacy and effectiveness for specific seizure or epileptic syndrome (Table-1)
- II. Dosing frequency and Cost (Table-2)
- III. Mode of actions (Table-3)
- IV. Pharmacokinetic properties (Table-4)
- V. Safety and tolerability profile (Table-4)
- VI. Patient's circumstances

13.1 A systematic approach to the long-term pharmacological treatment of epilepsy is recommended^[24]

- a. Establish the diagnosis of epilepsy and the need for long term AEDs
- b. Start with a single AED after deciding on the type of seizure(s) and the epilepsy syndrome
- c. Begin with a low dose and increase gradually
- d. Counsel and educate the patients and care givers about his/her epilepsy and treatment. This information can be provided by doctors treating the patients or a nurse trained in epilepsy care.
- e. Review the patients within a month to

assess compliance; side effect and seizure control.

- f. Review every 6 to 8 weeks. If the seizures are not controlled and there are no side effects increase the dose appropriately. In about 60 - 70% of patients, these steps are sufficient to achieve good seizure control.
 - If the AED fails to control seizures:
 - Review the diagnosis and seizure pattern
 - Review compliance (see also "drug monitoring")
 - Ensure that the maximum dosage has been used
- g. If the first AED continues to be ineffective at the maximum tolerated dose, introduce an alternative AED slowly without tapering the first.
- h. If the patient has a good response to the second AED, consider withdrawing the original AED gradually.
- i. Consider long-term two-drug therapy if mono therapy has not achieved remission or good seizure control.
- j. If the first add-on AED is ineffective, or produces undesirable side effects, withdraw it slowly and simultaneously replace it with a second add-on AED from the remaining choices. This process can be repeated for other possible add-on AEDs.
- k. If the seizures are still not adequately controlled on two AEDs, some patients may benefit an additional third AED.

14.0 When & how to stop anti-epileptic drug treatment

58-58

14.0 When & how to stop anti-epileptic drug treatment^[25]

Overall view is that, there is no fixed time limit, but majority recommends considering other factors at least 2 years' seizure free with drugs is necessary to stop drug. For some special situation long term drug treatment is necessary. When AED treatment is being discontinued in a child, young person or adult who has been seizure free, it should be carried out slowly (at least 2-3

months) and one drug should be withdrawn at a time. Particular care should be taken when withdrawing benzodiazepines and barbiturates (may take up to 6 months or longer) because of the possibility of drug-related withdrawal symptoms and / or seizure recurrence.

15.0 Recommended AED according to seizure type or Epilepsy syndrome

60-63

15.1 Recommended drugs for Bangladesh by SNB

63

15.0 Recommended AED according to seizure type or epilepsy syndrome^[26]

Table-1
According to Seizure Type

Seizure Types	Mono therapy	Adjunctive therapy* (Other than drugs in immunotherapy)	Therapy for resistant cases
Focal Seizures	Carbamazepine** Lamotrigine Levetiracetam Oxcarbazepine** Zonisamide Sodium valproate***	Clobazam Gabapentin** Topiramate Perampanel Lacosamide Phenobarbital Phenytoin**	Eslicarbazepine Pregabalin** Tiagabine** Vigabatrin**
Generalized Tonic Clonic seizure only	Sodium valproate*** Lamotrigine Carbamazepine** Oxcarbazepine**	Clobazam Levetiracetam Topiramate Perampanel	

Seizure Types	Mono therapy	Adjunctive therapy* (Other than drugs in immunotherapy)	Therapy for resistant cases
Absence Seizures	Ethosuximide Sodium valproate*** Lamotrigine		Clobazam Levetiracetam Clonazepam Topiramate Zonisamide
Myoclonic Seizures	Sodium valproate*** Levetiracetam Topiramate		Clobazam Clonazepam Piracetam Zonisamide
Tonic or Atonic Seizures	Sodium valproate***	Lamotrigine	Rufinamide Topiramate
Infantile spasm	Steroid Vigabatrin** (1 st for tuberous sclerosis)		

According to Epilepsy Syndrome

Epilepsy Syndrome	Mono therapy	Adjunctive therapy* (Other than drugs in immunotherapy)	Therapy for resistant cases
Dravet Syndrome	Sodium valproate*** Topiramate	Clobazam Stiripentol	
Lennox–Gastaut Syndrome	Sodium valproate***	Lamotrigine	Rufinamide Topiramate Felbamate
Benign epilepsy with centrottemporal spikes, Panayiotopoulos syndrome or late-onset childhood occipital epilepsy (Gastaut type).	Carbamazepine** Lamotrigine Levetiracetam Oxcarbazepine** Sodium valproate***	Clobazam Gabapentin** (Carbamazepine** and Oxcarbazepine** may exacerbate or unmask CSWS, which may occur in BCECTS.) Phenobarbital Phenytoin**	Eslicarbazepine Lacosamide Pregabalin** Tiagabine** Vigabatrin** Zonisamide
Idiopathic Generalized Epilepsy	Sodium valproate*** Lamotrigine Topiramate	Perampanel	Clobazam Clonazepam Zonisamide
Juvenile Myoclonic Epilepsy (JME)	Sodium valproate*** Lamotrigine (may exacerbate myoclonic seizure) Levetiracetam Topiramate		Clobazam Clonazepam Zonisamide
Childhood absence epilepsy, juvenile absence epilepsy or other absence epilepsy syndromes	Ethosuximide Sodium valproate*** Lamotrigine		Clobazam, Clonazepam Levetiracetam Topiramate Zonisamide

15.1 Based on socioeconomic condition, affordability of our patients and for drug compliance, Society of Neurologists of Bangladesh (SNB) recommends these drugs for Bangladesh:

For focal seizure:

- Carbamazepine** 
- Oxcarbazepine** 
- Phenobarbital  (N.B. Should be offered where compliance due to cost is suspected)
- Phenytoin **  (N.B. Should be offered where compliance due to cost is suspected)
- Topiramate 
- Lamotrigine 
- Sodium valproate*** 
- Levetiracetam 

For generalized epilepsy:

- Sodium valproate*** 
- Levetiracetam 
- Lamotrigine 
- Carbamazepine** 
- Topiramate 
- Phenobarbital (N.B. Should be offered where compliance due to cost is suspected) 

*Medications in the monotherapy column will be suitable adjunctive as well if the first medication effect is suboptimum.

**Do not offer Carbamazepine, Gabapentin, Oxcarbazepine, Phenytoin, Pregabalin, Tiagabine or Vigabatrin for patient with idiopathic generalized epilepsy, absence seizures, myoclonic seizures, tonic or atonic seizures, Lennox Gastaut Syndrome, Dravet syndrome.

*** Use of Sodium valproate in female of childbearing age needs special consideration

 Recommended drugs for our country by society of neurologists of Bangladesh

16.0 Dosing frequency

65-74

16.1	Modes of action of AEDs	68-69
16.2	AEDs pharmacokinetics & adverse reactions	70-73
16.3	Key messages and special recommendations for specific drugs	73-74

16.0 Dosing frequency^[27]

AED	Usual Daily Dose	No. of doses/day
Carbamazepine	Initial: 100 mg (Adults); 5 mg/kg/day (Children). Maintenance: 400-1600mg/day(Adults); 10-20 mg/kg/day (Children)	2-3
Oxcarbazepine	Initial: 600 mg/day (Adults); 10 mg/kg/day (Children) Maintenance: 1200-2400mg/day(Adults); 20-40mg/kg/day Children)	2
Eslicarbazepine	Initial: 400mg/day(Adults); Maintenance: 800-1200 mg/day (Adults)	1
Clobazam	Initial: 5-10 mg/day (Adults); 0.1 mg/kg/day (Children) Maintenance: 10-20 mg/day (Adults); 1 mg/kg/day (Children)	2
Ethosuximide	Initial: 250-500 mg/day (Adults); 5-10 mg/kg/day (Children) Maintenance: 750-2000mg/day(Adults); 20-40 mg/kg/day (Children)	2-3
Pregabalin	Initial: 150 mg/day (Adults) Maintenance: 150-300 mg/day (Adults)	2
Lamotrigine	Initial: 25mgEOD (With Valproate) (Adults) 0.15 mg/kg/day (With Valproate), 0.3 mg/kg (Without Valproate) (Children) Maintenance: 100-200mg/day(With Valproate) 100- 400mg/day (Without Valproate)(Adults) 1- 3mg/kg(With Valproate), 4.5-7.5 mg/kg/day(Without Valproate) (Children) Adjunctive therapy with Valproate: Gradual increment in the dose over one month (Adults). Higher doses if concurrent enzyme inducer.	1-2

AED	Usual Daily Dose	No. of doses/day
Phenobarbitone	Initial:30mg/dayMaintenance:30-180mg/day(Adults);3-5mg/kg/day (Children)	1-3
Primidone	Initial:100-125mg/day(Adults)Maintenance:750-1500mg/-day(Adults)	1-3
Phenytoin	Initial: 200-300 mg/day (Adults.); 5 mg/kg/day (Children) Maintenance: 300-400 mg/day (Adults), 5-8 mg/kg/day (Children)	1
Topiramate	Initial: 25-50 mg/day (Adults), 0.5-1 mg/kg/day (Children) Maintenance:200-400 mg/day (Adults); 3-9 mg/kg/day (Children)	2
Valproate	Initial: 400-600 mg/day (Adults); 10-15 mg/kg/day (Children) Maintenance: 400-2500 mg/day (Adults); 20-40 mg/kg/day (Children under 20 kg); 20-30 mg/kg/day (Children over 20 kg).	2
Vigabatrin*	Initial: 1000 mg/day (Adults), 50 mg/kg/day (Children); Maintenance:1.5-3g/day(Adults),100-150 mg/kg/day (Children)	2
Felbamate*	Maintenance: 2400-3600 mg/day, 45 mg/kg/day (Children) Maintenance: 2400-3600 mg/day, 45 mg/kg/day (Children)	3-4
Tiagabine*	Initial: 4 mg/day, Maintenance: 32-56 mg/day	1-4
Rufinamide*	Initial: 400 mg/day (Adults), 10 mg/kg/day (Children) Maintenance: 1800 mg/day (Adults), 45 mg/kg/day (Children)	2
Ezogabine*	Initial:300mg/day(Adults);Maintenance: 600-1200 mg/day (Adults)	3
Zonisamide	Initial: 100 mg/day (Adults), 1 mg/kg/day (Children) Maintenance:300-400mg/day (Adults), 12 mg/kg/day(Children)	1-2
Lacosamide*	Initial:100mg/day (Adults); Maintenance: 200-400 mg/day (Adults)	2

AED	Usual Daily Dose	No. of doses/day
Perampanel*	Initial: 2mg nocte, 4 mg nocte if concurrent enzyme inducer (Adults) Maintenance: 8-12 mg nocte (Adults)	1
Levetiracetam	Initial: 500mg/day (Adults), 14-20 mg/kg/day (Children) Maintenance: 1000-3000mg/day (Adults); 40-60mg/kg/day Children	2
Brivaracetam*	The recommended starting dose for monotherapy and adjunctive therapy is 50 mg twice daily (100 mg/day) and is initiated without titration. Based on individual patient response, the dose may be adjusted between 25 mg twice daily (50 mg/day) and 100 mg twice daily (200 mg/day).	2
Divalproex sodium*	The dose of Divalproex sodium to treat epilepsy as monotherapy should be initiated at 10 to 15 mg/kg/day. The recommended starting dose of Depakote to treat migraines is 250 mg twice daily	2
Rufinamide*	The recommended starting daily dose of rufinamide in adults with Lennox-Gastaut Syndrome is 400 mg per day to 800 mg per day administered in two equally divided doses	2
Safinamide*	Start with 50 mg administered orally once daily at the same time of day; after two weeks, the dose may be increased to 100 mg once daily, based on individual need and tolerability	1
Fosphenytoin	The dose of IV fosphenytoin (15 to 20 mg PE/kg) that is used to treat status epilepticus is administered at a maximum rate of 150 mg PE/min. The typical fosphenytoin infusion administered to a 50 kg patient would take between 5 and 7 minutes.	1
Stiripentol*	The dosage is 50 mg/kg/day, administered by mouth in 2 or 3 divided doses	2-3
Felbamate*	Adults (≥ 14 years): begin with 1,200 mg daily given every 6 to 8 hours Children (2–14 years): 15 to 45 mg per kg per day given every 6 to 8 hours	2-3

* * Not available in Bangladesh"

16.1 Modes of action of AEDs [28]

AED	Ion Channel	Excitatory Mechanism	Inhibitory Mechanism	Others
First Generation				
Benzodiazepine			Enhances GABA	
Carbamazepine	Na, Ca (L-type) blockade			
Ethosuximide	Ca (T-type) blockade			
Phenobarbitone	Increases chloride ion influx		Enhances and increases GABA	
Phenytoin	Na blockade			
Valproic acid	Na/Ca (T-type) blockade		Enhances GABA	
Second Generation				
Felbamate	Na/Ca blockade	Antagonises NMDA receptors		
Gabapentin	Ca (N-, P/Q-type) blockade			
Lamotrigine	Na/Ca (N-, P/Q-, R-, T-type) blockade		Increases GABA	
Levetiracetam	K ⁺ /Ca (N-type) blockade		Increases GABA	Binds to SV2A Protein
Oxcarbazepine	Na/Ca (N- and P-type) blockade			

AED	Ion Channel	Excitatory Mechanism	Inhibitory Mechanism	Others
Rufinamide	Na prolonged inactivation			
Tiagabine			Increases GABA	
Topiramate	Na blockade	Antagonises AMPA/kainate glutamate receptor	Enhances GABA	Inhibits carbonic anhydrase enzyme
Vigabatrin			Increases GABA	
Zonisamide	Na/Ca (N-, P-, T-type) blockade			Inhibits carbonic anhydrase enzyme
Third Generation				
Ezogabine/Retigabine	K (enhances M-type current)			
Lacosamide	Increases slow inactivation of Na channels			Binds to collapsin response mediator protein-2
Perampanel		Antagonises AMPA glutamate receptor		

16.2 AEDs pharmacokinetics and adverse reactions ^[29]

Oral AED	Oral Bioavailability	Half-life	Side effects
Phenobarbitone	Good	80-100H	Sedation, decreased concentration, depression, hyperactivity (children), reduced bone density, plantar fibromatosis, Dupuytren contracture Frozen shoulder.
Primidone	Good	10-15H	Similar to phenobarbitone, acute toxic reaction with debilitating drowsiness, dizziness, ataxia, nausea and vomiting.
Phenytoin	Variable	- >42H (dose dependent longer in Toxicity)	Ataxia, incoordination, dysarthria, nystagmus, diplopia, gingival hypertrophy, hirsutism, a paradoxical increase in seizures in overdose, hypotension, arrhythmias, purple glove syndrome.
Carbamazepine	Good	25-65H (initial use) 8-22H (auto induction)	Blurred vision, diplopia, nystagmus, unsteadiness, in- coordination, tremor, hyponatremia, weight gain, decreased bone density, mild leukopenia, rarely aplastic anemia. Rash and SJS (increased risk with HLA B1502)
Oxcarbazepine	Good	1-4H, 8 – 10H (active metabolite, prolonged in renal important)	Drowsiness, headache, fatigue, dizziness, blurred vision, diplopia, nausea, vomiting and ataxia, rash (25% cross reactivity with CBZ), more hyponatremia than CBZ.
Eslicarbazepine	Good	13-20H	Similar to oxcarbazepine. Less hyponatremia, rash 3%.

Oral AED	Oral Bioavailability	Half-life	Side effects
Valproate	Good	13-16H	Gastric irritation with nausea, vomiting, anorexia, fatigue, drowsiness, tremor, weight gain, hair loss, peripheral oedema, thrombocytopenia. Encephalopathy and hyperammonemia in polypharmacy (TPX, ZNS). Idiosyncratic hepatotoxicity and pancreatitis.
Ethosuximide	Good	30-60H	GI adverse effect, neuropsychiatric disturbances. Idiosyncratic reaction includes rash, SJS, SLE, aplastic anemia, thrombocytopenia, agranulocytosis, and rarely autoimmune thyroiditis.
Clobazam	Good	36-42H, 71-82 (active metabolite)	Drowsiness, nystagmus, incoordination, unsteadiness, dysarthria.
Clonazepam	Good	17-60H	Same as clobazam
Felbamate	Good	20-23H	GI irritability, insomnia, weight loss, aplastic anemia (1/5000 to 1/8000), hepatic failure (1/26,000 to 1/54,000)
Gabapentin	Low	5-7H	Drowsiness, dizziness, ataxia, tiredness, weight gain, myoclonus, cognitive slowing in the elderly, emotional lability in children, peripheral oedema.
Pregabalin	Good	~6H	Same as GBP
Lamotrigine	Good	~24H, double with valproate	Dizziness, blurred vision, diplopia, unsteadiness, nausea and vomiting, headache, tremor, rash 3%, TENS and SJS (1/4000)

Oral AED	Oral Bioavailability	Half-life	Side effects
Topiramate	Good	~21H	Cognitive adverse effects including cognitive slowing, decreased attention and memory, impaired executive function, word finding difficulty and reduced verbal fluency, sedation, fatigue, dizziness, ataxia and depression, kidney stones 1.5%, paresthesia, weight loss, glaucoma, oligohidrosis, hyperthermia and metabolic acidosis may occur in children.
Tiagabine	Good	7-9H	Dizziness, asthenia, nervousness, tremor, depression and emotional lability. Dose-related nonconvulsive status epilepticus or encephalopathy.
Levetiracetam	Good	6-8H	Somnolence, dizziness, asthenia, limitability and hostility (esp. children), depression.
Zonisamide	Good	~60H	Cognitive slowing and difficulty with concentration, depression and psychosis SJS, TEN rarely, kidney stones 4%, oligohidrosis, hyperthermia and metabolic acidosis (esp. children), aplastic anemia.
Lacosamide	Good	~13H	Dizziness, headache, nausea, vomiting, diplopia, fatigue, sedation, cardiac arrhythmias.
Vigabatrin	Good	10.5H	Sedation, fatigue, dizziness, ataxia, irritability, behavior changes, psychosis depression, weight gain, progressive and permanent bilateral concentric visual field constriction (30 % to 40%)

Oral AED	Oral Bioavailability	Half-life	Side effects
Rufinamide	Good	6-10H	Dizziness, fatigue, somnolence and headache, short QT interval.
Ezogabine / retigabine	Limited	7-11H	Dizziness, somnolence, fatigue, confusion, blurred vision, tremor, and nausea, weight gain, urinary retention 2%, bluish pigmentation in the skin, nails and retina.
Perampanel	Good	105H	Dizziness, somnolence, headache, fatigue, ataxia and blurred vision, aggression and hostility.

16.3 Key Messages and Special Recommendations for Specific Drugs

- AED should be started after establishing the diagnosis and need for long term AEDs; the patient and the caregiver must participate in the discussion process.^[30]
- Choice of AED is highly individualized based on the efficacy, safety, mode of actions, cost and pharmacokinetics of the AED, the seizure type(s) and epilepsy syndrome as well as the patient's preference.^[30]
- There are special considerations for the use of sodium valproate in women of child bearing age.^[30]
- Major indications for AED monitoring are:
 - To check compliance.
 - To determine if signs or symptoms are the result of AED toxicity.
 - As a guide to dosing of certain AEDs (in particular, phenytoin).
- To monitor pharmacokinetic interactions. As a guide in certain situations e.g. pre-pregnancy planning, during pregnancy, and status epilepticus.^[30]
- Withdrawal of AEDs after a period of remission should be clearly discussed with patients and their caregivers.^[30]
- The latency of carbamazepine-induced SJS/TEN is 25 to 90 days.^[30]
- Special care must be taken when using generic AEDs in patients with refractory epilepsy and those who are on polytherapy. These patients are best maintained on patented AEDs to prevent seizures.^[30]
- Carefully consider the risk-benefit ratio when using vigabatrin because of the risk of an irreversible effect on visual fields.^[31]
- If the person has myoclonic seizures or is suspected of having juvenile myoclonic epilepsy (JME), be aware that lamotrigine may exacerbate myoclonic seizures.^[31]

10. Offer a steroid (prednisolone or tetracosactide) or vigabatrin as first-line treatment to infants with infantile spasms that are not due to tuberous sclerosis. Carefully consider the risk–benefit ratio when using vigabatrin or steroids.^[31]
11. Offer sodium valproate as first-line treatment to children with Lennox–Gastaut syndrome.^[31]
12. Offer lamotrigine as adjunctive treatment to children, young people and adults with Lennox–Gastaut syndrome if first-line treatment with sodium valproate is unsuitable, ineffective or not tolerated.^[31]
13. Offer carbamazepine or lamotrigine as first-line treatment to children and young people with benign epilepsy with centrotemporal spikes, Panayiotopoulos syndrome or late-onset childhood occipital epilepsy (Gastaut type).^[31]
14. Offer sodium valproate as first-line treatment to children, young people and adults with newly diagnosed JME, unless it is unsuitable.^[31]
15. Offer lamotrigine or sodium valproate as first-line treatment to children, young people and adults with epilepsy with GTC seizures only. If they have suspected myoclonic seizures, or are suspected of having JME, offer sodium valproate first, unless it is unsuitable.^[31]
16. Offer ethosuximide or sodium valproate as first-line treatment to children, (young people and adults) with absence syndromes. If there is a high risk of GTC seizures, offer sodium valproate first, unless it is unsuitable.^[31]
17. Do not offer carbamazepine, gabapentin, oxcarbazepine, phenytoin, pregabalin, tiagabine or vigabatrin for patients with idiopathic generalized epilepsy, absence seizures, myoclonic seizures, tonic or atonic seizures, Lennox-Gastaut Syndrome and Dravet syndrome.^[30]

17.0 Surgical treatment of epilepsy

76-77

17.1	Definition of epilepsy surgery	76
17.2	Indication of epilepsy surgery	76
17.3	Contra-indication of epilepsy surgery	76
17.4	Refractory epilepsy	76

17.0 Surgical treatment of epilepsy

17.1 Definition of epilepsy surgery

- Epilepsy surgery is defined as surgery carried out specifically to control epileptic seizures.
- The term epilepsy surgery also implies a particular mindset and a specific approach to pre-surgical assessment.

17.2 Indication of epilepsy surgery:

- Medically refractory epilepsy

17.3 Contra-indication of epilepsy surgery:

17.3.1 Absolute:

- Primary generalized epilepsy.
- Minor seizures but do not impair the quality of life (QOL)

17.3.2 Relative:

- Progressive medical or neurologic disorder
- Active psychosis, not related to peri-ictal period
- Behavioral problems that impair rehabilitation
- IQ<70 (for local resective surgery only)
- Poor memory functions in hemisphere contra lateral to the epileptic focus.

17.4 Refractory epilepsy:

There is no accepted uniform definition for intractability.

17.4.1 Definition:

Drug resistant epilepsy may be defined as failure of adequate trials of two tolerated and appropriately chosen and used AED schedules (whether as monotherapies or in combination) to achieve sustained seizure freedom.^[32]

Patient with uncontrolled seizures or those who develop intolerable side effects that interfere with their QOL, despite maximally tolerated trials of one or more AEDs are considered to have refractory epilepsy.

17.4.2 Criteria:

For how long the patient should have uncontrolled seizures or what should be the frequency of seizures to designate intractability varies from patient to patient.

17.4.3 Factors considered in the decision making process for refractoriness are-

- Patient's expectation.
- The degree of disability due to seizures or AED toxicity.
- Aversion to AED intake.
- Employment.
- Marriage.
- Difficulty to obtain drinking license.

In general, patients who continue to exhibit two or more disabling seizures per month for a period of two years or more despite supervised trials (six months each) twice with mono therapies and once with poly therapy are considered refractory.

17.4.4 Factors associated with resistance to AED therapy:

- Onset in infancy.
- Organic brain damage.
 - Mental retardation.
 - Neurologic signs.
 - Cerebral palsy.
- Seizure type- Tonic, atonic and myoclonic seizures
- Multiple seizure types.
- High seizure frequency.
- Long duration of uncontrolled seizure.
- Failure of past AED treatments.
- Abnormal (epileptic form) EEG.

Pseudo refractory epilepsy:

- Diagnostic error.
- Inadequate dosage of AED.
- Inappropriate assessment.
- Patients lack of cooperation.

18.0 Comprehensive epilepsy care program

79-79

- | | | |
|------|--|----|
| 18.1 | Functions of comprehensive epilepsy care program | 79 |
| 18.2 | Types of surgical procedures of intractable epilepsy | 79 |

18.0 Comprehensive epilepsy care program

18.0 Comprehensive epilepsy care program:

Patients having intractable epilepsy can benefit significantly from a systematic, comprehensive diagnostic and therapeutic reevaluation program.

18.1 Functions of comprehensive epilepsy care program

- Evaluation of epileptic patient.
- Pre-surgical evaluation.
- Epilepsy surgery.
- Community-based epilepsy care.
- Therapeutic trials.
- Group counseling & epilepsy education.
- Basic science research.

- Gross removal of malfunctioning brain tissue-
- Multi lobar resections
- Hemispherectomy

18.2.2 Functional operations:

- Division of pathways of spread
- Corpus callosotomy
- Division of epileptogenic neuronal aggregate
- Multiple subpial transections (MST)
- Focal ablation
- Focal stimulation
- Vagus nerve stimulation (VNS)

18.2 Types of surgical procedures for intractable epilepsy:

18.2.1 Resective operations:

- Removal of an epileptic focus or discrete lesion-
 - Focal corticectomy
 - Gyrectomy
 - Lesionectomy
 - Anterior temporal lobectomy (ATL)
 - Selective amygdalohippocampectomy (AH)
 - ATL+AH

19.0 Emergency management of epilepsy

81-82

- | | | |
|------|--|-------|
| 19.1 | Initial supportive management for compulsive seizure | 81 |
| 19.2 | Get patient to the nearest hospital | 81 |
| 19.3 | Emergency AED therapy needed | 81-82 |

19.0 Emergency management of epilepsy

19.0 Emergency Management of Epilepsy

Typically, seizures are fewer than 5 minutes in duration and self-limiting. Mean duration of GTCS is 62 seconds and focal seizure with impaired awareness is 120 seconds. In most cases of GTCS, treatment is usually supportive and do not require emergency treatment. Patients will recover fully after a period of rest of about 30-60 minutes.^[33]

19.1 Initial supportive management for convulsive seizure (Seizure First Aid)^[34]

During an acute epileptic seizure, the patient should be made as comfortable as possible.

The following general measures should be taken:

- Note the time the seizure started and time until it ends.
- Place the patient on a smooth surface, if possible.
- Protect the head – if available use a pillow or cushion.
- Remove any harmful/hard objects that could cause injury.
- Loosen tight clothing or neckwear released.
- Do not attempt to restrain the person or stop the jerking.
- Avoiding placing/putting any objects in the patient's mouth.

- As soon as possible roll the person onto their side– may need to wait until the seizure movements have ceased. Turn the patient to the left (or right), if left not and place head on a soft support (bundle of cloth or pillow).
- Talk to the person to make sure they have regained full consciousness.
- Stay with and reassure the patient until he or she recovers fully, and gather information about the patient's background and epilepsy history.

19.2 Get patient to the nearest hospital if^[33,34]

- Seizure persisted beyond 5 minutes or longer than is customary for individual patient.
- There is no recovery of consciousness after 30 minutes,
- Seizure rapidly recur
- Recent increase in seizure frequency
- Serious injury has occurred
- Significant fever
- The cardiorespiratory system is impaired.

19.3 Emergency AEDs therapy needed for^[33, 35]

- Prolonged seizure: Lasting 5 minutes and more

- Acute repetitive seizures (serial seizures): Three or more seizures in an hour, with full recovery between attacks.
- Status epilepticus: A seizure activity lasting 5 minutes or longer or two or more discrete seizures between which there is incomplete recovery of consciousness.
 - Convulsive status epilepticus either 5 minutes or more of continuous seizure activity or two or more discrete seizures between which there is incomplete recovery of consciousness.
 - Nonconvulsive status epilepticus a condition when electrographic seizure activity persisted for greater than 30 minutes in absence of visible convulsion.

20.0 Treatment for prolonged seizure

84-85

20.1 Prolonged seizures & acute repetitive seizure

84

20.0 Treatment of prolonged seizures^[33, 36]

In the event that the seizure does not stop after 5 minutes following measure should be taken

- Vital parameters including respiration, BP, heart rate, oxygen saturation and ECG must be monitored
- Maintained the patient in left lateral position.
- Airway must be patent and possibility of rapid sequence ET intubation considered.
- Intravenous access must be established.
- The respiratory rate and pattern is observed.
- Oxygen is delivered through high flow mask.
- If there is any suspicion of hypoglycemia as the cause of seizure 50ml of 50% glucose should be given intravenously.
- In addition, if Wernicke's encephalopathy is suspected, an intravenous bolus of thiamine 100 mg should be given prior to glucose administration.

20.1 Prolonged seizure and acute repetitive seizures (serial seizures)

Prolonged seizure and acute repetitive seizures (serial seizures) may be aborted by benzodiazepines. Intravenouslorazepam or diazepam is the principal first line AEDs used for prolonged seizure.

Dose:

Diazepam: 0.15mg/kg @2.5mg/min over <5minutes max 10 mg or

Lorazepam: 0.1-15mg/kg over 1-2 minutes; max 4 mg

20.1.1 Alternative to parenteral benzodiazepines^[33]

- When intravenous access is difficult, alternative routes of BDZ administration are rectal, buccal and intranasal.
- Rectal diazepam 0.2-0.5mg/kg (maximum 20mg).
- Buccal or intranasal Midazolam 0.2 mg/kg (IV 5mg/ml solution)

Rectal Diazepam dosing according to age

2-5 years	0.5mg/kg
6-11 years	0.3mg/kg
>11years or more	0.2mg/kg

20.1.2 Treatment algorithms for convulsive status epilepticus ^[35]

0-5 Minutes	Stabilize patient (Airway, breathing, circulation, disability) Finger-stick glucose IV access and blood work If there is any hypoglycemia as the cause of seizure 100ml of 25% glucose should be given intravenously.
5-20 Minutes	Benzodiazepine administration IM midazolam (10mg if >40kg) IV lorazepam (0.1mg/kg/dose, maximum 4mg/dose) IV diazepam (0.15-0.2 mg/kg/dose, maximum 10mg) Can be repeated after 15 minutes if seizure continues or recur
20-40 Minutes	Second AED IV fosphenytoin (20mg/kg maximum 1500mg) IV Phenytoin, 20mg/kg at 50mg/min IV levetiracetam (60mg/kg, maximum 4500mg) IV Valproate sodium (40mg/kg, maximum 3000mg) Or if none available, IV phenobarbital (15mg/kg).
40-60 Minutes	Third therapy phase Repeat second-line therapy or Anesthetic doses of Thiopental (2-7mg/kg; administer at an infusion <50mg/min) Midazolam (0.2mg/kg; infusion rate of 2mg/min) Pentobarbital (5-15mg/kg; administer at an infusion rate <50mg/min) Propofol (20mcg/kg/min with 1-2mg/kg loading dose) with continuous EEG monitoring Patient should be managed in ICU.

20.1.3 Management during post status phase

Maintenance therapy:

All AEDs that were used to treat the status should be continued on maintenance dosage till remains seizure free for at least 3-7days if patient awake, if GCS remain low gradually remove under EEG coverage.

AED therapy must be given in parallel with emergency treatment. The choice of drug depends on previous therapy, the type of epilepsy and clinical setting. Any pre-existing AED therapy should be continued at full dose, and any reductions reversed.^[37]

21.0 Epilepsy in special situations

87-94

21.1	Epilepsy in women	87
21.2	Epilepsy & menstruation	87
21.3	Fertility & epilepsy	88
21.4	Contraception	88
21.5	Pre-conception management & counseling	89
21.6	Monitoring during pregnancy for mother & fetus	90
21.7	Management during labour	91
21.8	Lactation	91-92
21.9	Driving & epilepsy	93
21.10	Eclampsia & other hypertensive conditions	93
21.11	Anticoagulation	93
21.12	AEDs in hepatic disease	93
21.13	AEDs in renal disease	94
21.14	Obesity & AEDs	94
21.15	Epilepsy in elderly	94

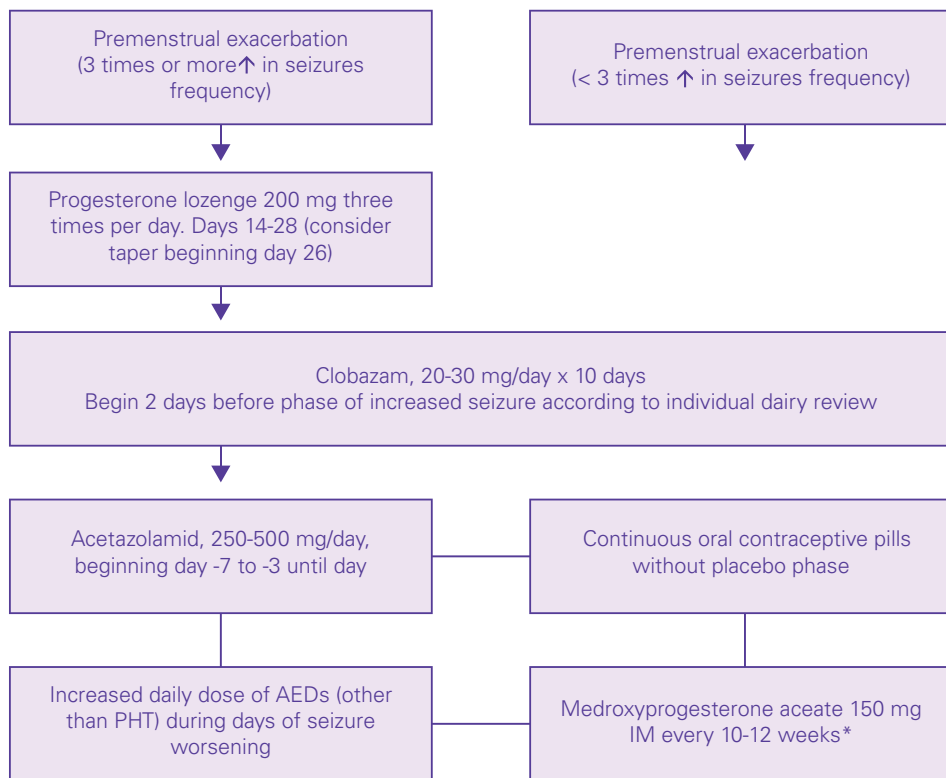
21.0 Epilepsy in special situations

21.1 Considered issues included

- Epilepsy in women
 - Epilepsy & Menstruation
 - Fertility
 - Contraception
 - Pre-conception management and counseling
 - Monitoring during Pregnancy for mother and fetus
 - Lactation
 - Eclampsia and other hypertensive conditions
 - Driving & epilepsy
 - Anticoagulation & epilepsy
 - AEDs in renal and hepatic disease
 - Obesity and AEDs
 - Epilepsy in elderly
- Women with epilepsy have disturbance in luteinizing hormone concentration, pulsatile release and in oestrogen and progesterone hormone levels
 - About one third women with epilepsy (WWE) have an abnormal menstrual cycle length (less than 23 days or more than 35 days)
 - There is a higher prevalence of PCOS in patients on valproate as compared to other AEDs.^[38]
 - Catamenial exacerbations occur in 78% of women with epilepsy
 - First line treatment catamenial exacerbations is temporally increasing the baseline AEDs dose
 - In adjunction acetazolamide 250 to 1000 mg/d for 10 to 14 days starting at mid cycle if fluctuations or natural progesterone lozenges 300 to 800 mg/d during the second half of the cycle tapering over 2 to 3 days after onset of menses.^[39]

21.2 Epilepsy & menstruation

- Menstrual disturbances are as high as 20-60% of epileptic women



* Considered only if catamenial exacerbations are severe & intractable to other interventions.

Figure 3 Treatment algorithm for catamenial (Perimenstrual) Pattern of seizures^[39]

21.3 Fertility & epilepsy

- The fertility rate for WWE is up to 33% lower than expected.^[40]

Probable several reasons are:

- Social factors: WWE are less likely to marry & have children
- Sexual factors: Epilepsy & anti-epileptic drugs can interfere with sexual desire & arousal
- Physical factors:
 - Epilepsy & antiepileptic drugs can interfere with fertility
 - WWE more likely to develop PCOS especially with sodium valproate
 - Temporal lobe epilepsy has three times more anovulatory cycle than women without epilepsy^[52]

21.4 Contraception

- Enzyme inducer AEDs increase metabolism & thereby decreased concentration of estrogen and progestogens which may result in contraceptive failure.^[40]
- WWE taking enzyme inducer AEDs should choose
 - Combined oral contraceptive pill
 - 50 micrograms of oestrogen
 - 75 micrograms or 100 micrograms levonorgestrol (if break through bleeding occurs)
 - Tricycling' (taking three packs without a break)
 - Depot injections of progesterone
 - 10 weeks instead of 12 wks
- Valproate, levetiracetam, gabapentin, clobazam & lamotrigine are safe AEDs in patient taking OCP. However, combined oral pill tend to lower the lamotrigine level and therefore higher lamotrigine level may be required.^[41]
- WWE taking enzyme inducing AEDs should avoid progesterone-only pill, progesterone implants, contraceptive patches, vaginal rings^[42]

Emergency contraception in WWE^[55]

- levonorgestrel should be increased to 1.5 mg and 750 micrograms 12 hours apart
- IUCD including IUD progesterone

21.5 Pre-conception management and counseling

- Psychological well-being of the patient should be considered before planning a pregnancy

- Ideally, women should be advised against getting pregnant until they become seizure free.^[43]
- WWE should not be discouraged from becoming pregnant, as chances of having a healthy baby is more than 90%.^[40]
- Women should be reassured that increase seizure frequency is generally not common in pregnancy or in the first few months after birth^[44]
- In untreated women with epilepsy, there is no risk of congenital malformations in the off-spring
- Risk of teratogenicity while on AEDs and risk of recurrent seizures, status epilepticus, SUDEP and spontaneous abortion in case of discontinuing of AEDs must be discussed long before women wish to conceive.^[44]
- The latter risk is low if the patient has been seizure-free for more than 2 years and tapering may be done gradually
- Switching to a less teratogenic AED should be done before conception
- Switching during pregnancy is likely to be pointless because most teratogenic effects take place in the first trimester
- Contraception should be practiced till AEDs adjustment is achieved
- If an epileptic patient is on AEDs seen in the first time at first trimester and if there is rare attack or complete seizure free, no need to change or dose modification of the ongoing AED
- Initiation of polytherapy to monotherapy of appropriate type should be validated ideally before six months of conception
- Sustained release formulations of AEDs at lowest possible doses

- AEDs treatment should be optimized well before conception
- Prophylactic folic acid supplements should be given.^[56]

21.6 Monitoring during Pregnancy for mother and fetus

- Teratogenic risk in newer generation is low
- Recurrent seizures during pregnancy is more harmful than the risk of teratogenicity with AEDs
- Monotherapy at lowest possible dose to achieve satisfactory seizure control should be considered
- Medication changes should be avoided once conception has occurred
- Sustained release formulations of AEDs are preferable at the lowest possible doses
- Incidence of MCM increased with polytherapy and with increased drug concentrations
- Levetiracetam, lamotrigine and oxcarbazepine monotherapy has lower risk of malformations than sodium valproate and others.
- Rate of neural tube defects more in valproate but less in carbamazepine.^[45]
- Prophylactic folic acid is recommended to avoid teratogenicity.^[45]
- Usually suggested dose 2.5-5 mg/day, three months before conception and continuing up to the 12 weeks of gestation.^[45]
- Measurement of blood concentrations of AEDs can be useful to titrate the dose. It should be done in each trimester and in the last month of pregnancy
- Drugs with extensive protein binding (Phenytoin, Phenobarbital, Carbamazepine and Valproate), free plasma concentration should always be measured
- The level of many AEDs decline by average of 50% during third trimester of pregnancy & an increase in dosage is recommended during this time.
- Drug dosage should be reduced to pre-pregnancy dosage within 10 days after delivery.^[53]
- Aims to identify any major malformations as early as possible
- High resolution transvaginal ultrasonography between 18 -20 weeks to detect structural anomalies
- Reassure patient that >90% pregnancies proceed with no problem in women with epilepsy
- WWE without AEDs treatment do not have increased risk of having children with malformation/Teratogenicity
- Occurrence of GTCS during pregnancy carries risk for the mother and the fetus.^[44]
- But there is no clear evidence that partial, absence or myoclonic seizures adversely affect pregnancy / fetus.^[45]
- Oxcarbazepine monotherapy during pregnancy don't show an increased risk of malformations
- Incidence of MCM has been reported to increase with polytherapy and with increasing serum drug concentrations.^[39]
- Precaution should be taken about neonatal hemorrhage
- Enzyme inducing AEDs (phenytoin or carbamazepine) can accelerate the metabolism of vitamin K, leading to a relative deficiency of this vitamin in neonates

- This deficiency is associated with a potentially increased risk of bleeding.
- This risk does not exist for all AEDs such as valproate or gabapentin that don't induce CYP enzyme
- Maternal intake of vitamin K (10mg/day orally) during the last month of pregnancy is recommended^[46]
- It is recommended that vitamin K (1 mg IM or IV) should be given to all newborns postpartum to avoid coagulation defects.^[47]

21.7 Management during labour

- Continue AED (IV if required)
- If high risk of seizures- Benzodiazepine is the drug of choice (e.g. clobazam 10-20mg)
- If seizures occur during labour - cesarean section^[54]
- There is no contraindication to regional or spinal anesthesia^[53]

21.8 Lactation

- Breast-feeding for most women on AED is generally safe^[50]
- Antiepileptic drug secretion in breast milk is inversely proportionate to the extent of protein binding
- Phenytoin, carbamazepine and valproate excreted poorly in milk
- Overall, antiepileptic drug concentrations in blood samples of infants who were breastfed are substantially lower than maternal blood concentrations.
- Given the well-known benefits of breastfeeding and as the studies demonstrated no ill effects when the mother was receiving antiepileptic drugs, breastfeeding of infants by mothers with epilepsy who are taking antiepileptic drug therapy should be supported.^[57]

Management algorithm of Women with Epilepsy (WWE) in pregnancy

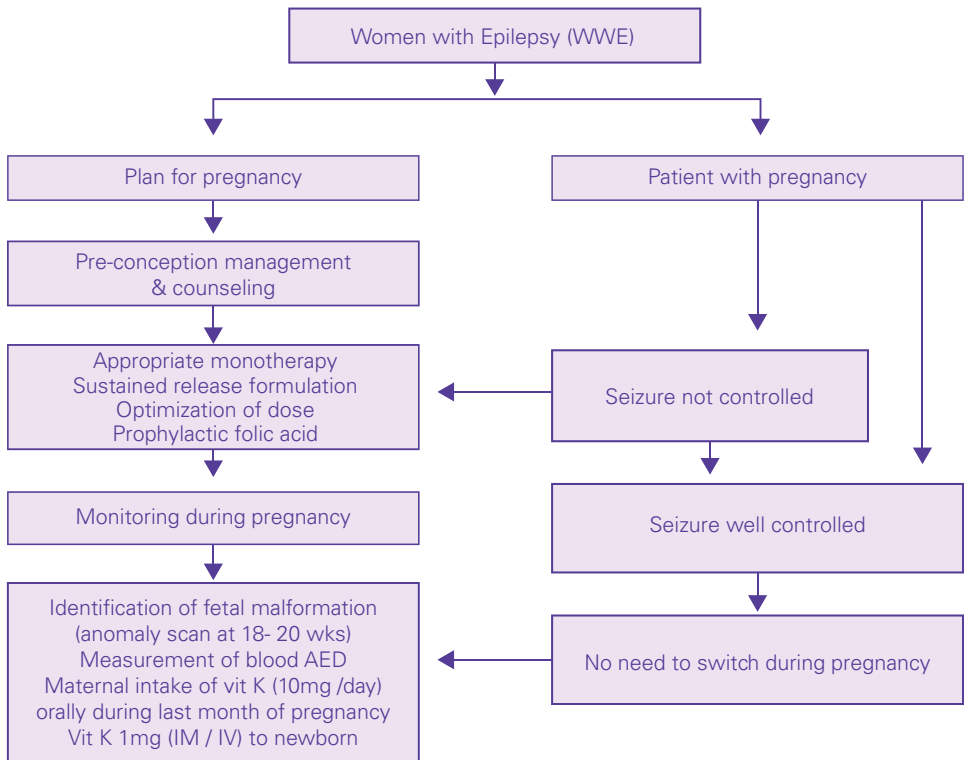
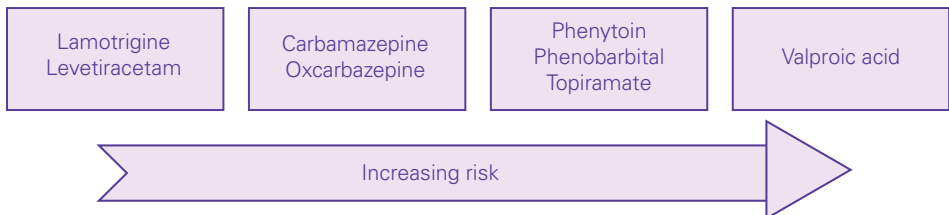


Figure 4 Management algorithm of Women with Epilepsy (WWE) in pregnancy

Teratogenic risk profiles of antiepileptic drugs ^[48]



21.9 Driving & epilepsy^[58]

- Stop driving for 1 year if recurrence within 1 year
- License restored
 - when patient is free from all types of seizure for 1 year
 - Seizures exclusively during sleep for a period of 3 years
- License will require renewal every 3 years thereafter (until 10 seizure-free years)
- Patient who is newly diagnosed and being started on medication is advised to stop driving for 6 – 12 months, until the seizures have stabilized and any drug-related side effects have settled
- Obtaining driving licenses in these situations is clearly not possible in driving heavy machinery (tractors and public buses, flying commercial or military airplanes)

21.10 Eclampsia and other hypertensive conditions

- Women with epilepsy have an increased risk of mild pre-eclampsia, but not for the severe types of hypertensive pregnancy complications.^[59]
- Intravenous magnesium is the mainstay of treatment. One regimen is a 4-g load, followed by continuous infusion of 2–4 g per hour, to maintain a level of 4–8 mg/dL till seizure controlled
- When hypertension is clearly a causal factor, rapid control of blood pressure using labetalol or nitroprusside is recommended

21.11 Anticoagulation

- Stroke treatments sometimes need to be modified because of the coexistence of seizures or the use of AEDs
- Enzyme-inducing AEDs (phenytoin, carbamazepine, and phenobarbital) produce major increases in warfarin metabolism, so that warfarin doses must be adjusted when these AEDs are initiated or withdrawn, or when major dose changes are made.^[60]
- Furthermore, warfarin may be contraindicated if seizures are not completely controlled and if chance of fall is present
- Alternative treatments, such as adjusted subcutaneous heparin or low-molecular-weight heparin preparations carry similar risk of serious bleeding in those prone to falls or other trauma
- Antiplatelet agents have lower risk but also lower efficacy in stroke prevention for those with atrial fibrillation. Antiplatelet agents must be used with caution in patients on valproate.^[61]

21.12 AEDs in hepatic disease:^[49]

- Levetiracetam and topiramate can be given safely but dose reduction is needed in severe hepatic disease (child Pugh C).
- Gabapentine & pregabalin can be given in usual dose.
- Valproate and lamotrigine should be avoided.
- Carbamazepine, phenytoin and Phenobarbital can be used in reduced dose.

21.13 AEDs in renal disease:^[49]

- Carbamazepine, phenytoin and valproate can be given in usual dose.
- Dose reduction is needed in case of Levetiracetam, topiramate, lamotrigine and oxcarbazepine.

21.14 Obesity and AEDs^[62]

- Weight gain caused by antiepileptic drugs (AEDs) constitutes a serious problem in the management of people with epilepsy.
- AEDs associated with weight gain include sodium valproate, pregabalin and vigabatrin.
- Excessive weight gain can lead to non-compliance with treatment and to an exacerbation of obesity-related conditions.

21.15 Epilepsy in elderly^[50]

- Late onset epilepsy is common.
- Stroke & occult vascular disease is a common (30-50%) cause of seizure in elderly. Ten percent are due to metabolic causes. Subdural hematoma is an underdiagnosed cause of epilepsy in elderly people.^[51]

- Antiepileptic drug regimen should keep as simple as possible.
- Take care to avoid interaction with other drug.
- Carbamazepine induced hyponatremia increases significantly with age (particularly in patient on diuretic or those with heart failure).
- Drug withdrawal should be attempted considering risk benefit ratio.

22.0 Management of pediatric epilepsy

96-112

22.1	Epileptic encephalopathy	96
22.2	Epileptic syndrome	96-97
22.3	Epileptic syndrome: neonatal onset	98-99
22.4	Infantile spasm	99-101
22.5	Treatment with Intramuscular Acth	102
22.6	Treatment with oral Prednisolone UKISS protocol	102
22.7	Treatment with oral Vigabatrin	102
22.8	Severe Myclonic Epilepsy of infancy/ Dravet Syndrome	103
22.9	Natural course of Dravet Syndrome	104-106
22.10	Epilepsy with Myclonic Atonic Seizure (Doose Syndrome)	106-107
22.11	Lennox - Gastaut Syndrome (LGS)	107
22.12	Difference among common childhood epileptic syndromes	108
22.13	Landau-Kleffner syndrome (LKS)	108
22.14	Treatment	109
22.15	Genetic epilepsy with febrile seizure plus- GEFS+	109
22.16	Self-limited epilepsies of childhood	109
22.17	Panayiotopoulos syndrome	109-110
22.18	Clinical & EEG features of main self-limited Childhood epilepsies	110-111
22.19	Childhood absence	111
22.20	Childhood absence: ILAE criteria	111
22.21	Febrile seizure	112
22.22	Defined by ILAE	112
22.23	National Institute of Health Consensus	112
22.24	Classification of febrile seizure	112

22.0 Management of Pediatric Epilepsy

The principle of treatment of epilepsy is same both in children and adults. The treatment of common epileptic disorders is outlined earlier. The following section outlines the diagnosis and management of epilepsy syndrome which are more common in children.

22.1 Epileptic Encephalopathy^[63]

The term epileptic encephalopathy is used to describe epilepsies in which epileptic activity itself is believed to contribute to a progressive decline in cognitive and behavioral function above and beyond what would be expected from the underlying pathology alone and may present as epileptic encephalopathy.

The epileptic encephalopathy is contributed by medically intractable seizures and/or epileptiform discharges.

Many specific structural, genetic, metabolic causes for epileptic encephalopathy are identified. Evaluation may be time consuming, must not delay treatment. For this reason, epileptic syndromes are distinguished.

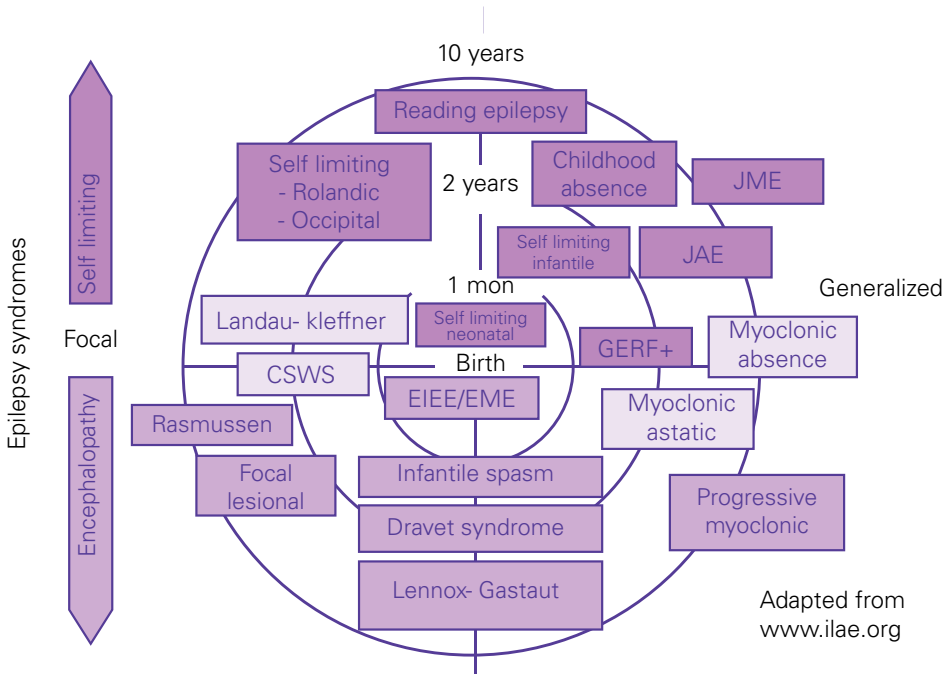
22.2 Epileptic Syndrome^[64]

An epilepsy syndrome is a disorder characterized by a cluster of symptoms and signs customarily occurring in combination.

Diagnosis of epileptic syndrome depends on clinical presentation and investigation findings that varies from one syndrome to another. Classically it should include:

- Clinical: Age of onset, seizure type, recurrence, Inter - ictal condition, family history, neurological & psychological findings, prognosis.
- Investigations: EEG, CT, MRI

As per ILAE classification of common syndromes are categorized in different age groups like birth-1month, 1 month- 2 years, 2-10 years and beyond (Figure as follows)



So Epileptic Syndrome are presented below as tabulated form based on age of presentation

Epileptic Syndromes : 1-2 yrs of age	
First months:	• Early Infantile Epileptic Encephalopathy (EIEE / Ohtahara) • Early Myoclonic Epilepsy
1st year	• Infantile Spasm • Severe Myoclonic Epilepsy (Dravet Syndrome) • Benign Familial / + Non-familial Seizures • Myoclonic Astatic Epilepsy (Dooze Syndrome)
First 3 years	• Benign Myoclonic Epilepsy
Variable	• Generalized Epilepsy with Febrile Seizure + (GEFS+) • Hemiconvulsive - hemiplegia -epilepsy
Epileptic Syndromes: 2-12 years' age Group	
Benign	• Benign Partial Epilepsy of Childhood with Centro-temporal Spikes • Benign Occipital Epilepsy • Intermediate • Childhood Absence Epilepsy (CAE) • Generalized Epilepsy with Febrile Seizure Plus (GEFS+)
Catastrophic	• Lennox- Gastaut Syndrome (LGS) • Landau-Kleffner Syndrome (LKS) • Myoclonic Astatic Epilepsy • Continuous Spikes Wave in Slow Sleep (CSWS)

22.3 Epileptic Syndrome: Neonatal Onset^[65]

Early onset epileptic encephalopathies with burst suppression (EOEE-BS): Previously described EIEE and EME, which are recently been considered part of a spectrum, with overlap in clinical presentation and etiology.

- Common characteristics
 - Neonatal onset

- EEG: suppression burst
- Seizure intractability
- Developmental regression/stagnation
- Causes of EOEE-BS
 - Brain malformations (e.g., polymicrogyria and lissencephaly)
 - Inborn errors of metabolism (e.g., pyridoxine- and other vitamin-dependent epilepsies, mitochondrial disorders, and amino acidopathies)

- Other genetic etiologies (e.g., pathogenic variants in ARX, KCNQ2, SCN2A, SIK1, SLC25A22, STXBP1)
- Clinical differences between EIEE and EME

Character	Early myoclonic encephalopathy (EME)	Early infantile epileptic encephalopathy (EIEE)
Onset	Neonatal: 1 st wk 76%, by 1m 96%	1-3 months, mainly neonatal
Seizure type	Myoclonic	Tonic spasm
Aetiology	IEM	Anoxia, cerebral dysgenesis
	Only in sleep	Both in awake & sleep
Evolution	West syndrome	West syndrome, LGS
Treatment	Benzodiazepam	ACTH, B ₆ , CZP, LEV, ZSM, VBG, ↑ dose PB
Outcome	Refractory to Rx	Refractory to Rx

- Treatment: EOEE-BS

Management option for EIEE:

- Anti-seizure drugs (limited efficacy): BDZ, high dose Phenobarbitone[65](15 mg/kg/day), phenytoin, LEV, TPM, VPA, Vigabatrin, pyridoxine
- ACTH/corticosteroid: less effective
- Ketogenic diet: after excluding contraindicated metabolic cause
- Correction of underlying metabolic cause

- Surgery: For focal brain malformation
- Targeted therapy:
STXBP1 mutation: LEV
KCNQ2 mutation: Sodium channel blocker (CBZ, VPA, ZNS, TPM, Phenytoin), Potassium channel openers (Retigabine)
KCNT1 mutation: Quinidine

Management of EME:

- Treatment of underlying metabolic disorder
- Ketogenic diet: Non ketotichyperglycinaemia
- Pyridoxine/ pyridoxal phosphate
- Anti-epileptic drugs

- Prognosis^[66]

EIEE: Poor prognosis

EME: Extremely poor prognosis

- Mortality: 50% die within 2 years
- Psychomotor stagnation or progressive deterioration → vegetative state

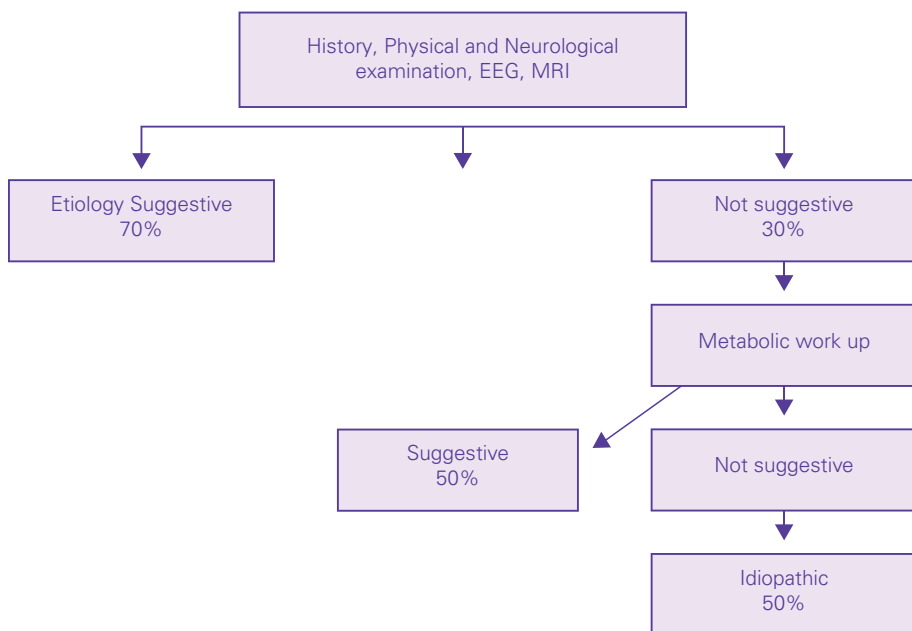
22.4 Infantile Spasm

Devastating form of epilepsy defined by a triad of infantile spasm, hysarrhythmia and developmental regression.

22.4.1 Clinical presentation (ILAE - 1992)

- Spasm characterized by symmetric clusters of flexor, extensor, or mixed axial jerks
- No. of spasm: 2-100
- Duration of spasm: 2-10 secs
- Occurs in clusters
- Duration of cluster : < 1 min – 10 min
- Peak age: 3-7 months

- **Infantile spasm: etiological evaluation**



- **Infantile Spasm: Metabolic work-up:^[67]**

Basic metabolic screening like estimations of Arterial blood gas, Serum lactate, Blood ammonia, Urine for ketone bodies which ideally should be done 4 hours after fasting. Further Urine metabolic screen includes: Ferric chloride test, DNPH (Dinitrophenyl hydrazine test), Nitroprusside, Reducing substance. Followings are the further metabolic condition that may require further test.

- Pyridoxine Dependent Seizure
- Biotinidase Deficiency
- Plasma amino acids: MSUD, PKU
- Plasma ammonia: Hyperammonemia disorders
- Serum pyruvate & lactate
- Urine for organic acids: Organic acidemia
- CSF: Amino acids, lactic acids, glucose, folate, glycine, neurotransmitters
- Chromosomal studies: Down, Miller-Decker syndrome
- Gene mutations: ARX, CDKL5

- Treatment: Infantile spasm

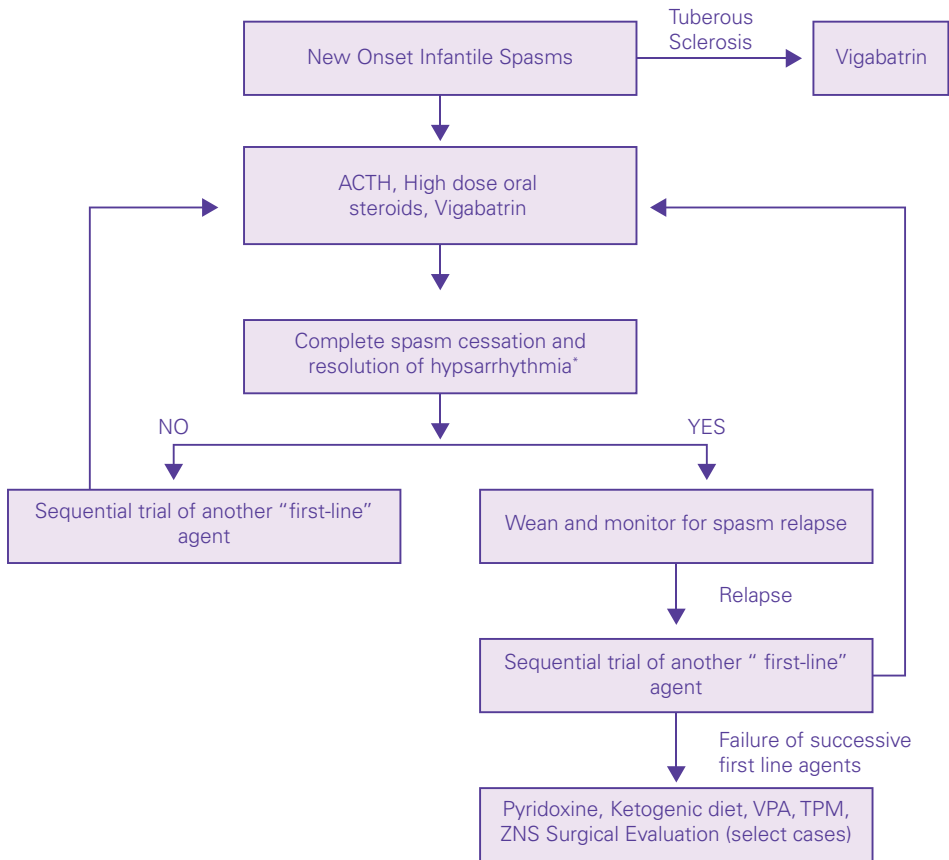


Figure 5 Treatment pathway for new onset infantile spasm

1st line treatment: ACTH, High dose corticosteroid, Vigabatrin

2nd line treatment: conventional anti-seizure medication, ketogenic diet

22.5 Treatment with intramuscular ACTH^[68]

If there is no clinical response by day 14, consider alternative treatment.

Days	Dose-ACTH
1-14	75 U/m2 twice daily#
15-17	30 U/m2 in the morning
18-20	15 U/m2 in the morning
21-23	10 U/m2 in the morning
24-29	10 U/m2 every other morning (3 total doses)

22.6 Treatment with oral Prednisolone UKISS protocol^[69]

Days	Dose-Prednisolone
1-14	10 mg oral 4 times daily*#
15-19	10 mg oral 3 times daily*
20-24	10 mg oral 2 times daily
25-29	10 mg oral daily

* If there is no clinical response after day (i.e. no 24-hour period free of infantile spasms), the dose can be increased to 20 mg three times daily. If done, the taper schedule from day 15-19 would be 10 mg 4 times daily and then proceed as in the table beginning on day 20.

If no clinical response by day 14, consider alternative treatment

22.7 Treatment with oral Vigabatrin^[80]

Days*#	Dose-Vigabatrin
1-3	50 mg/kg/day divided 2 times daily
4-6	100 mg/kg/day divided 2 times daily
>7	150 mg/kg/day divided 2 times daily

If no clinical response by day 14, consider alternative treatment.

* International collaborative Infantile Spasm Study (ICISS) showed, new onset Infantile Spasm receive Combination therapy (ACTH+ Vigabatrin) exhibit superior response.

22.8 Severe Myclonic epilepsy of infancy / Dravet Syndrome:

22.8.1 Evolution EEG and clinical stages in patients with Dravet syndrome

First stage (1-12 months)	
•	Seizures mainly convulsion, long-lasting, febrile. Hemiclonic seizures are characteristic of Dravet syndrome
•	Normal EEG and MRI
•	Normal development
Second stage (12-15 months to 5 years)	
•	Polymorphous pharmacoresistant seizures: myoclonia, atypical absence, tonic-clonic seizures and focal seizures
•	Gait disturbance
•	Cognitive slowing with attention deficit, behavior and autism features in some
•	EEG normal or showing slowing in the background with rare spikes
Third stage (>6 years)	
•	Pharmacoresistant seizures persisting with a few seizure-free patients
•	Nocturnal seizures are more frequent than diurnal
•	Definite cognitive decline without regression

22.9 Natural course of Dravet syndrome^[71]

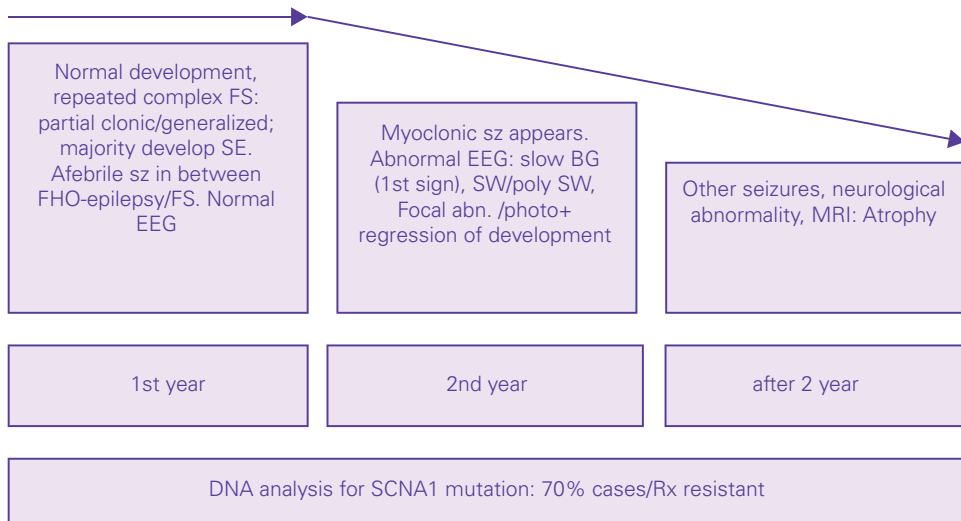


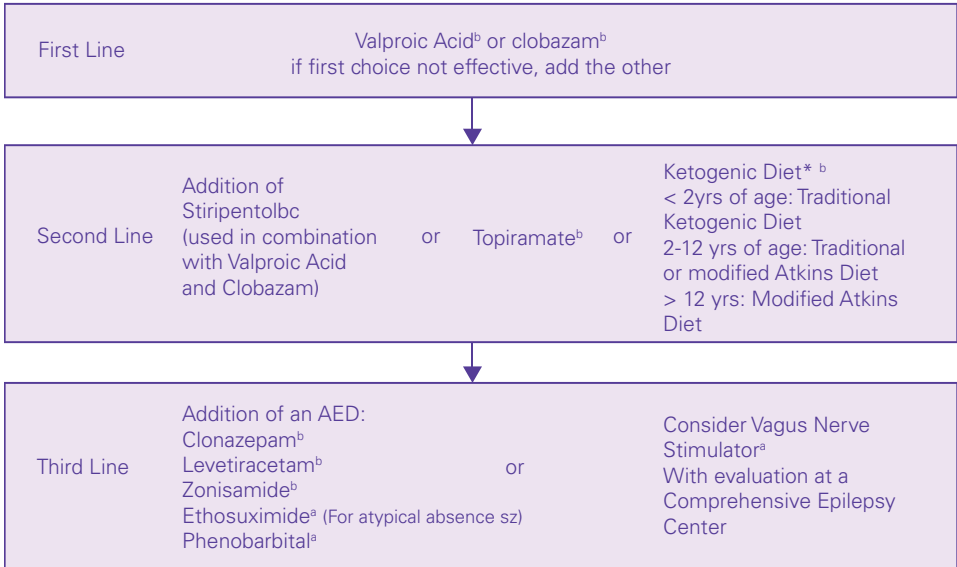
Figure: Natural course of Dravet syndrome

- Treatment - SME:

Anti-seizure drugs:

- VPA→BDZ (Clonazepam/Clobazam)
- TPM (Focal Seizure)
- Refractory GTCS: Stiripentol (50mg/kg/day 2to 3 divided dose→3000mg/day) adjuvant therapy with VPA and BDZ
- Other AED (adjuvant therapy): LEV, Ethosuximide, ZND, Bromide
- Drugs might worsen seizure: CBZ, LTG, PHT, VEG
- Cannabidiol and Stiripentol are FDA approved drugs for Dravet syndrome
- Cannabidiol (Epidiolex): Initial 2.5mg/kg BD→ Maintenance 5mg/kg BD → Max 10mg/kg BD
- Fenfluramine, Fluxetine, Varapramil: Orphan drugs for Dravet syndrome

Management algorithm of Dravet syndrome is as follows^[72]



Prescribing Information for Cannabidiol and Stiripentol			
Generic Name Brand name (Approval Date)	Formulations	Labeled Indications	Labeled Dosage
Cannabidiol Epidiolex1 (June 2018)	Oral Solution: 100 mg/ml	Treatment of seizures associated with Lennox-Gastaut syndrome or Dravet syndrome in patients 2 years of age and older	- Initial dosage: 2.5 mg/kg twice daily - Maintenance dosage after 1 week: 5 mg/kg twice daily - Maximum recommended maintenance dosage: 10 mg/kg twice daily - Dose adjustments in hepatic impairment
Stiripentol Diacomit2 (August 2018)	Oral capsule: 250 mg and 500 mg Powder for Oral suspension: 250 mg and 500 mg	Treatment of seizures associated with Dravet syndrome in patients 2 years of age and older taking clobazam. There are no clinical data to support the use of Diacomit as monotherapy in Dravet syndrome	50 mg/kg/day in 2 or 3 divided doses - Maximum recommended dosage: 3,000 mg/day

Utahmedical drug report march 2019^[73]

- Possible efficacy: Fenfluramine (1.5-3 mg/kg/day), Verapamil, Fluoxetine

22.10 Epilepsy with Myclonic atonic seizure (Dooze syndrome)^[74]

- Diagnostic criteria of EMAS
 - Seizure onset in a previously normal child between age 1-5 years
 - Absence of structural brain anomalies
 - Strong genetic context, with high incidence of seizure or epilepsy in the family
- Myoclonic-atonic seizures resulting in drops and falls, associated with multiple generalized seizure type: myoclonic, atonic, ansence, GTCS; less commonly tonic seizures, as well as nonconvulsive status epilepticus and spasm
- Variable response to medication, possible appearance of behavioral and cognitive impairment in some patients
- Variable prognosis for epilepsy and cognition, ranging from excellent to poor

- EEG criteria (ILAE 1989)^[75]
 - Initially: Normal / Theta BG
 - Later on: Generalized polyspike & wave discharges
 - Photosensitivity with 4-7hz spike-wave complexes
 - Normal Posterior BG rhythms
 - Normal sleep changes in EEG always present
- Treatment of EMAS^[75]
 - Multiple AEDs: SVA, LTG, CZP, ZNS, TPM, LEV single /combination
 - Steroid: ACTH, Pred or Dexamethasone 1mg/Kg
- Prognosis: favorable or unfavorable
 - Normal cognition → severe intellectual disability
 - Seizure freedom → intractability
- Age: 1- 8 years (Preschool)
- High seizure frequency
- Status epilepticus is common
- Steps for Evaluating LGS^[76]
 - Video EEG
 - MRI of brain: cerebral malformation (Focal cortical dysplasia, Subcortical band, heterotopia, Perisylvian polymicrogyria, Hypothalamic hamartoma)
 - Metabolic screening
 - Genetic/ chromosomal microarray (SLC2A1 for GLUT, CLN2 for infantile NCL, TSC1,2 for Tuber sclerosis)
- LGS –Treatment
 - VPA ± LTG, ± TPM, ± Benzodiazepam (CLB / CZP/ NZP)
 - Adjunctive: LEV, ZNS, Rufinamide, ACTH
 - Ketogenic diet, VNS
 - Surgical therapies

22.11 Lennox- Gastaut syndrome (LGS)

The most common form of epileptic encephalopathy with (1) Multiple seizure types (2) Cognitive impairment and (3) The interictal EEG: Slow spike (Typically 1-2.5Hz, usually generalized and occasionally multifocal)

- LGS: Diagnostic criteria-ILAE^[76]
 - Severe epileptic seizure (Atypical absences, axial tonic seizure, and sudden atonic or myoclonic falls)
 - Diffuse slow inter-ictal spike wave in the awaking EEG (< 3HZ) , fast rhythmic bursts (10 HZ) during sleep
 - Slow mental development associated with personality disturbances

22.12 Difference among common childhood epileptic syndromes

Character	BME	SME	MAE	LGS
Age of onset	1 st 3yr of life	1 st yr of life	7m – 6 years , 94% within 5Y	2-8 years
Dev. before Sz onset	Normal	Normal dev.& cognition	Normal	Always delayed esp. cognition
Fever ppt.Sz	Absent	Yes	Yes	Absent
Predominant Sz	Myoclonic ,brief	Starts with partial→Myoclonic , Any Sz can develop	Myoclonic –astatic , Multiple Seizure	Axial tonic Sz, Multiple Sz
Tonic Seizure	None	±	Only in sleep	Awake & sleep
Status epilepticus	Uncommon	Majority	Common	Electrical SE during: slow-wave sleep
Pre-existing neurological deficit	None	None	None	Always
EEG	Generalized Poly SW	SW / Poly SW Focal abnormality Photosensitivity	Initially : Normal / Theta BG, Later on: Generalized Poly SW	Abn. BG, slower (2–2.5Hz) SW runs for prolonged periods
MRI	Normal	Normal at onset	Normal	Always abnormal

22.13 Landau- Kleffner Syndrome (LKS)^[77]

22.13.1 Clinical presentation:

- Develop normally
- Rapid loss of receptive and expressive language skills > age 3
- Acquired developmental aphasia
- Auditory agnosia
- 70% of children with LKS have clinical seizures at any time
- EEG in stage III sleep: continuous spike-wave discharge even in absence of clinical seizure.
- Awake EEGs: normal /diffuse slowing and/ or intermittent isolated epileptiform events

22.14 Treatment

22.14.1 Treatment options:

- Standard AEDs
- Corticosteroids (ACTH/ Prednisolone)
- High dose Benzodiazepines (1mg/kg max 40mg on day 1 then 0.5mg/kg for 3-4 weeks → slowly tapered 2.5mg/month → maintenance 2.5-10mg for 2 years, if no improvement then rapid tapering)
- IVIG
- Epilepsy Surgery
 - Early corticosteroid treatment has been considered the treatment of choice for LKS
 - In general, if AEDs do not work then either high dose diazepam or corticosteroids are used

6-month dosing schedule for oral Prednisolone^[78]

2 mg/kg/day for 1 month (maximum dose 60mg)

1.5 mg/kg/day for 1 month

1 mg/kg/day for 1 month

1 mg/kg/day every other day for 1 month

0.75 mg/kg every other day for 1 month

0.5 mg/kg/day every other day for 1 month

22.15 Genetic Epilepsy with Febrile Seizure Plus – GEFS+

SCN1A seizure disorders encompass a spectrum that ranges from simple febrile seizures and GEFS+ at the mild end to Dravet syndrome at the severe end.

22.15.1 Clinical features

- Genetic cause: AD in inheritance
- Develop normally & remain same
- Feb. Seizure starts earlier (even 1m, median 1yr)
- Feb. Seizure persists beyond 6 years
- Other seizures beyond 6 years: Myoclonic, Focal, Atonic
- Strong FHO: FS /Afebrile Seizure including SME /MAE
- EEG: Normal Background, generalized slow wave discharge
- Seizures remit by mid-childhood (11 years)

22.15.2 Treatment: ^[79]

- Anti-seizure therapy according to seizure type.
- Sodium channel blockers may be potentially more problematic.

22.16 Self-limited epilepsies of Childhood:

- Panayiotopoulos syndrome
- Childhood Rolandic epilepsy
- Occipital epilepsy of Gastaut
- Benign childhood focal seizures associated with frontal spikes

22.17 Panayiotopoulos syndrome

Clinical features

- Age of onset: 3-6 years
- Occurs during sleep, including daytime naps
- Emetic symptoms: nausea, retching and vomiting

- Behavioral changes, particularly agitation
- Autonomic features: Pallor, Pupillary abnormality, urinary/ fecal incontinence, breathing change, tachycardia
- Seizure: Simple focal seizure, hemiconvulsion or GTCS, ictal syncope/ictal syncope like episode
- Generally prolonged (may last for 30 min): Autonomic status epilepticus
- EEG: Normal background with high amplitude, sharp and slow wave foci (functional spikes) in multiple location (characteristic findings of Panayiotopoulos syndrome)
- Treatment
 - Anti-epileptic drugs: When seizures are unusually frequent CBZ, VPA, LEV
- Prognosis
 - One third has a single seizure. >10 seizures (5-10%)
 - Remission usually occurs within 1-2 years from onset

22.18 The clinical and EEG features of the main self-limited childhood epilepsies^[80]

	Panayiotopoulos	Rolandic epilepsy	Occipital epilepsy of Gastaut
Age of onset	3-5 years	7-9 years	8-9 years
Sex prevalence	M=F	M>F	M=F
Seizure characteristics	Autonomic features with emesis Behavioral changes, particularly agitation Seizure: Simple focal, hemiconvulsion or GTCS	Focal sensorimotor to bilateral tonic clonic	Focal visual
Duration	Long (usually ≥ 9 min) Infrequent Mainly in sleep	Moderate (usually 2-4 min) Infrequent Mainly in sleep	Brief (sec-min) Frequent (sometimes daily) Mainly when awake
EEG	Multifocal spike	Centro temporal spike	Occipital spike

Treatment	CBZ, VPA (equally effective), LEV	CBZ, VPA, LEV, OXZ, gabapentin CBZ (theoretical risk of ↑ seizures EEG abnormality, worsening speech production)	CBZ, LEV
Prognosis	Excellent	Excellent	uncertain

22.19 Childhood Absence:

22.19.1 Main Clinical Characteristics:

- Age of onset: 4-10 years (peak 5-7 years)
- Abrupt impairment of consciousness without aura
- Accompanied by ≥1 additional features
 - Behavioral arrest/ arrest of activity, Staring spells
 - Eyelid fluttering and/or
 - Hand automatisms
 - No significant postictal confusion/ lethargy
 - Absence can be provoked by 3 minutes' hyperventilation in 80-90% cases
 - Duration of typical absence: 1-44 seconds
 - Can be very frequent, 100 times/day

22.20 Childhood absence: ILAE criteria

- Children of school age: 6-7 years
- Very Frequent seizures (Several to many per day)
- EEG: Normal background
- Bilateral synchronous, symmetrical, spike wave discharges, 3Hz
- Remit during Adolescent, persist (Rare),

GTCS may overlap.

22.20.1 EEG:

- Generalized, bilateral synchronous spike and wave complexes with frontal predominance. 3-4.5 Hz, in contrast to juvenile absence
- Gradual slowing of frequency from onset to termination
- Inter ictal background: Normal
- High voltage occipital intermittent rhythmic delta activity (OIRDA): 15-40%

22.20.2 Treatment:

- Anti-epileptic drugs:
 - Drug of 1st choice: Ethosuximide/VPA
 - Others: LTG, Clonazepam
 - Refractory to mono therapy: Ethosuximide+VPA
 - Other medication: BDZ(Clونazepam), TPM, Zonisamide,
 - Should avoid: CBZ, OXZ, PB, PHT, Tiagabine, Vigabatrin
 - In refractory cases one should exclude GLUT-1 deficiency both in children and adults

Prognosis: Excellent

22.21 Febrile Seizure

Though febrile seizure is not epileptic condition, considering its clinical importance, it is presented below.

22.22 Defined by ILAE

Seizure occurring in association with a febrile illness, in the absence of a central nervous system infection or acute electrolyte imbalance in children of older than 1 month of age without prior afebrile seizure.

22.23 National Institute of Health consensus

Onset: 3 month- 5years

- The febrile illness must include temp > 38.3 C, although the increased temperature may not occur until after seizure.

22.24 Classification of Febrile Seizure^[73]

- Simple febrile seizure: Isolated, brief, generalized tonic clonic, persist <15 min, no recurrence within 24 hours
- Complex (30%): Focal, prolonged (lasting for more than 15 minutes), or multiple (occurrence of more than one seizure during the febrile illness)
- Febrile status: Seizure persist >30min
- Approximately one third of the children with a 1st febrile seizure will experience a recurrence.
- 10% will have ≥3 recurrence
- Roughly 75% of recurrence occur with

1 years and 90% or more occur with 2 years. Frequency decreases after 3 years. Less than a tenth of the total risk of recurrence after 2 years.

Febrile seizure type	Recurrence risk
Simple febrile seizure	1%
Recurrent febrile seizure	4%
Complex febrile seizure	6%
Fever <1 hour before seizure	21%
Family history	18%
Complex (Focal) febrile seizure	20%
Neurodevelopmental abnormality	33%

22.24.1 Treatment^[71]

- Counselling regarding relative risk of recurrence of febrile seizure
- Acute management: BDZ: Per rectal Diazepam/ Lorazepam, Midazolam IV PHT, PB (Inc case of Febrile status) Antipyretics
- Preventive: Intermittent BDZ to prevent prolonged febrile seizure
 - Diazepam: 1mg/kg max 10 mg in 2 or 3 divided doses
 - Or Clobazam 1mg/kg (max 20mg) in 1 or 2 divided doses in 1st 3 days of febrile illness
 - Clobazam is preferable then Diazepam as it causes then Ataxia and drowsiness.
- Prophylaxis is not recommended.

23.0 Conclusion

Epilepsy is a common neurological disorder, but the treatment of epilepsy is not straightforward. It depends upon multiple domain including individual clinician's skill, knowledge and attitude, drug selection strategy like starting, switching and stopping capability, drug toxicity and interaction alert, compliance and follow up, patient and caregiver's awareness, social reaction to epilepsy-all these factors may play a crucial role in the management of epilepsy

At present there is no rational use of AEDs in epilepsy in our country. Improvement can occur if Clinical Practice Guidelines are introduced that addresses medical care of person with epilepsy which could be helpful resource for HCPs updating.

Lastly, this is actually a Clinical Practice Guideline. For introducing national epilepsy guideline evidence based study is mandatory which may be observational, cohort or RCT.

THIS DOCUMENT IS UNCLASSIFIED

DATE 08-11-2018 BY 60322 UCBAW/STW

REASON: 25X DOWNGRADING

DECLASSIFY ON: 25X DOWNGRADING

EXEMPTION CODE: 25X DOWNGRADING

EXEMPTION CODE: 25X DOWNGRADING

EXEMPTION CODE: 25X DOWNGRADING

EXEMPTION CODE: 25X DOWNGRADING

EXEMPTION CODE: 25X DOWNGRADING

EXEMPTION CODE: 25X DOWNGRADING

EXEMPTION CODE: 25X DOWNGRADING

EXEMPTION CODE: 25X DOWNGRADING

EXEMPTION CODE: 25X DOWNGRADING

EXEMPTION CODE: 25X DOWNGRADING

EXEMPTION CODE: 25X DOWNGRADING

EXEMPTION CODE: 25X DOWNGRADING

EXEMPTION CODE: 25X DOWNGRADING

24.0 Disclaimer

The National Epilepsy Consensus Guideline of Bangladesh presented here are developed to assist clinicians with decisions about appropriate health care for epileptic patients.

This guideline is targeted at clinicians only. This guideline does not constitute a textbook and therefore deliberately provide little, if any, explanation or background to the conditions and treatment outlined. They are however designed to acquaint the reader rapidly with the clinical problem and provide practical advice regarding assessment and management.

The recommendations contained in this guideline does not indicate an exclusive course of action or standard of care. They do not replace the need for application of clinical judgment to each individual presentation, nor variations based on locality and facility type.

The advisory board members and editorial board members of this guideline have made considerable efforts to ensure the information upon which they are based is accurate and up to date. Users of this guideline are strongly recommended to confirm that the information contained within them, especially drug doses, is correct by way of independent sources. The authors accept no responsibility for any inaccuracies, information perceived as misleading, or the success or failure of any treatment regimen detailed in the guideline.

The scientific partner, Sanofi Bangladesh Limited has offered only logistic and financial support during the formulation of the guideline. Sanofi did not show any intention and was not also involved in formulating any of the contents of this guideline.

References:

118-125

References:

1. Ngugi AK, Bottomley C, Kleinschmidt I, Sander JW, Newton CR: Estimation of the burden of active and life-time epilepsy: A meta-analytic approach. *Epilepsia* 2010, 51(5):883-890.
2. Ngugi AK, Kariuki SM, Bottomley C, Kleinschmidt I, Sander JW, Newton CR: Incidence of epilepsy: A systematic review and meta-analysis. *Neurology* 2011, 77(10):1005-1012.
3. Meyer AC, Dua T, Ma J, Saxena S, Birbeck G: Global disparities in the epilepsy treatment gap: A systematic review. *Bull World Health Organ* 2010, 88(4):260-266.
4. Mohammad QD, Saha NC, Alam MB et al. Prevalence of epilepsy in Bangladesh: Result from a national household survey. *Epilepsy Open*. 2020;5:526-536
5. Manan MA. Epilepsy in Bangladesh. *Neurology Asia: Epilepsy Association of Bangladesh & Neurology Foundation Dhaka, Bangladesh* 9 (Supplement): 18.
6. Gumnit RJ, Walczak TS: Guidelines for essential services, personnel, and facilities in specialized epilepsy centers in the United States. *Epilepsia* 2001, 42(6):804-814.
7. Labiner DM, Bagic AI, Herman ST, Fountain NB, Walczak TS, Gumnit RJ: Essential services, personnel, and facilities in specialized epilepsy centers—revised 2010 guidelines. *Epilepsia* 2010, 51(11):2322-2333.
8. Nunes VD, Sawyer L, Neilson J, Sarri G, Cross JH: Diagnosis and management of the epilepsies in adults and children: Summary of updated NICE guidance. *BMJ* 2012, 344: e281.
9. Juri K, Birbeck GL: Epilepsy care guidelines for low- and middle- income countries: From WHO mental health GAP to national programs. *BMC Medicine* 2012 10:107
10. Ehrhardt S, Meyer CG: Transfer of evidence-based medical guidelines to low- and middle-income countries. *Trop Med Int Health* 2012.
11. Fact Sheet: 10 facts on ageing and health; Epilepsy key factors. Avenue Appia 20, 1211 Geneva: World Health Organization. 7th February 2019

12. Fisher RS, Acevedo C, Arzimanoglou A, Bogacz A, Cross JH, Elger CE, Engel J Jr, Forsgren L, French JA, Glynn M, Hesdorffer DC, Lee BI, Mathern GW, Moshé SL, Perucca E, Scheffer IE, Tomson T, Watanabe M, Wiebe S. ILAE official report: A practical clinical definition of epilepsy. *Epilepsia*. 2014 Apr;55(4):475-82. doi: 10.1111/epi.12550. Epub 2014 Apr 14. PMID: 24730690.
13. Fisher RS, Cross JH, D'Souza C, French JA, Haut SR, Higurashi N, Hirsch E, Jansen FE, Lagae L, Moshé SL, Peltola J, Roulet Perez E, Scheffer IE, Schulze-Bonhage A, Somerville E, Sperling M, Yacubian EM, Zuberi SM. Instruction manual for the ILAE 2017 operational classification of seizure types. *Epilepsia*. 2017 Apr;58(4):531-542. doi: 10.1111/epi.13671. Epub 2017 Mar 8. PMID: 28276064.
14. Jean Bancaud(Paris), Olaf Henriksen(Oslo), Francisco Rubio-Donnadieu (Mexico City), MasakatusSenio (Shizuoka), Dreifuss, Chairman (Chariotteesvilla) et al. Proposal for revised clinical and electroencephalographic classification of epileptic seizures: 22(4), August 1981, p-489-501
15. Rudzinski LA, Shih JJ. The classification of seizures and epilepsy syndromes. *Continuum (MinneapMinn)*. 2010 Jun;16(3 Epilepsy):15-35. doi: 10.1212/01.CON.0000368230.11492.d5. PMID: 22810313.
16. Linda S. de Vries, Hannah C. Glass, *Handbook of Clinical Neurology: Practical Approach of Clinical Neurology: 3rd Series*, Elsevier, Volume 162, 2019, Pages v-vi
17. International League against Epilepsy (ILAE): *Epilepsy Imitators: Transient Global Amnesia (TGA)*; (Internet), [updated 2018; cited December 8, 2020] Available from: <https://www.ilae.org/education/diagnostic-manual>
18. Ralston S, Penman I, Strachan M, Hobson R. *Davidson's Principal and Practice of Medicine*. 23rd Edition. Edinburgh. UK: Elsevier; 2018.
19. Consensus Guideline on the Management of Epilepsy 2017, Epilepsy council: Malaysian Society of Neuroscience (Internet), MNS_ Guideline; 2017 [cited December 9, 2020]. Available from: https://www.neuro.org.my>MSN_Guideline_Consensus p-55
20. Malmgren K, Reuber M, Appleton R. *Oxford textbook of epilepsy & epileptic seizures*. United Kingdom (UK): Oxford University Press; 2012.

21. National Institute for Health and Care Excellence (NICE) guideline. Epilepsies: diagnosis and management (Internet), [London] NICE; 2018, [updated 2019 October; cited December 8, 2020] (clinical guideline [cg 137]). Available from: https://www.nice.org.uk/guideline/cg_137, p-18.
22. Siddiqui F, Sultan T, Mustafa S, Siddiqui S, Ali S, Malik A, Sajjad Z, Barech S, Jooma R, Epilepsy in Pakistan: National Guidelines for clinicians (Internet), [Pakistan] PJNS Epilepsy guideline; February 2017, [cited date December 10, 2020], special supplement, p-4
23. National Institute for Health and Care Excellence (NICE) guideline. Epilepsies: diagnosis and management (Internet), [London] NICE; 11 January 2012, [updated 2019 October; cited December 8, 2020] (clinical guideline [cg 137]). Available from https://www.nice.org.uk/guideline/cg_137, p-24, 25
24. Consensus Guideline on the Management of Epilepsy 2017, Epilepsy council: Malaysian Society of Neuroscience (Internet), MNS_ Guideline; 2017 [cited December 9, 2020]. Available from: https://www.neuro.org.my>MSN_Guideline_Consensus. p-27
25. National Institute for Health and Care Excellence (NICE) guideline. Epilepsies: diagnosis and management (Internet), [London] NICE; 11 January 2012, [updated 2019 October; cited December 8, 2020] (clinical guideline [cg 137]). Available from https://www.nice.org.uk/guideline/cg_137, p-37,
26. Consensus Guideline on the Management of Epilepsy 2017, Epilepsy council: Malaysian Society of Neuroscience (Internet), MNS_ Guideline; 2017 [cited December 9, 2020]. Available from: https://www.neuro.org.my>MSN_Guideline_Consensus. P-30-31,
27. Consensus Guideline on the Management of Epilepsy 2017, Epilepsy council: Malaysian Society of Neuroscience (Internet), MNS_ Guideline; 2017 [cited December 9, 2020]. Available from: https://www.neuro.org.my>MSN_Guideline_Consensus. P-32-33,
28. Consensus Guideline on the Management of Epilepsy 2017, Epilepsy council: Malaysian Society of Neuroscience (Internet), MNS_ Guideline; 2017 [cited December 9, 2020]. Available from: https://www.neuro.org.my>MSN_Guideline_Consensus. P-34
29. Consensus Guideline on the Management of Epilepsy 2017, Epilepsy council:

- Malaysian Society of Neuroscience (Internet), MNS_ Guideline; 2017 [cited December 9, 2020]. Available from: https://www.neuro.org.my>MSN_Guideline_Consensus. P-36-38
30. Consensus Guideline on the Management of Epilepsy 2017, Epilepsy council: Malaysian Society of Neuroscience (Internet), MNS_ Guideline; 2017 [cited December 9, 2020]. Available from: https://www.neuro.org.my>MSN_Guideline_Consensus. P-45
 31. National Institute for Health and Care Excellence (NICE) guideline. Epilepsies: diagnosis and management (Internet), [London] NICE; 11 January 2012, [updated 2019 October; cited December 8, 2020] (clinical guideline [cg 137]). Available from https://www.nice.org.uk/guideline/cg_137, p-29-34.
 32. Patrick khan, Alexis argimanoglove, Anne T. Berg, Martin J. Brodie, W. Allen Houser, Gray mathern, Soloman L. Mushe, Emilio Perucea, Samuel wibe, Jacqueline French. *Epilepsia* 2010, SI (6); p-1069-1077
 33. Malaysian society of neurology(MSN) guideline: Consensus guidelines on the management of epilepsy. Malaysia.2010. p-55
 34. Epilepsy Australia. Seizure first aid: tonic colonic seizure. North Ryde Be NSW 670. Australia.<http://www.epilepsyaustralia.net/seizure-first-aid/>
 35. Vanhaerents s, Elizabeth E. Gerard et. al. Epilepsy emergencies: status epilepticus, acute repetitive seizures and auto immune encephalitis, *Epilepsy, Continuum*. 2019 April;25(2): p: 454-76
 36. National Institute for Health and Care Excellence (NICE) guideline. Epilepsies: diagnosis and management (Internet), [London] NICE; 11 January 2012, [updated 2019 October; cited December 8, 2020] (clinical guideline [cg 137]). Available from https://www.nice.org.uk/guideline/cg_137, p- 44.
 37. National Institute for Health and Care Excellence (NICE) guideline. Epilepsies: Diagnosis and management (Internet), [London] NICE; 11 January 2012, [updated 2019 October; cited December 8, 2020] (clinical guideline [cg 137]). Available from https://www.nice.org.uk/guideline/cg_137, p- 83.
 38. Elaine Wyllie, Wyllie's Treatment of Epilepsy: Principles and Practice (6th edition),P-552
 39. Elaine Wyllie, Wyllie's Treatment of Epilepsy: Principles and Practice (6th edition), Editionp – 554 40

40. Randolph W. Evans MD et al. Saunders Manual of Neurologic Practice: February 7, 2003. P – 259
41. Wiley-Blackwell, Handbook of Epilepsy Treatment, 3rd Edition, ISBN: 978-1-405-19818-9, December 2010.P - 13842
42. National Institute of Health and Care Excellence (NICE) guideline: Epilepsies: diagnosis andmanagement: Clinical guideline [CG137], UK.11 January 2012, p – 44
43. National Institute of Health and Care Excellence (NICE) guideline: Epilepsies: diagnosis andmanagement: Clinical guideline [CG137], UK.11 January 2012, p – 47
44. National Institute of Health and Care Excellence (NICE) guideline: Epilepsies: diagnosis andmanagement: Clinical guideline [CG137], UK.11 January 2012, p – 45
45. National Institute of Health and Care Excellence (NICE) guideline: Epilepsies: diagnosis andmanagement: Clinical guideline [CG137], UK.11 January 2012, p – 43
46. Randolph W. Evans MD (Author). Saunders Manual of Neurologic Practice. February 7, 2003
47. National Institute of Health and Care Excellence (NICE) guideline: Epilepsies: diagnosis andmanagement: Clinical guideline [CG137], UK.11 January 2012, p – 46
48. Elaine Wyllie, Wyllie's Treatment of Epilepsy: Principles and Practice (6th edition), p – 566
49. Wiley-Blackwell, Handbook of Epilepsy Treatment, 3rd Edition, ISBN: 978-1-405-19818-9, December2010 p- 158-261
50. Stuart Ralston, Ian Penman, Mark Strachan, Richard Hobson,Davidson's Principles and Practice of Medicine, 23rd Edition, April 2018;p – 1103
51. Wiley-Blackwell, Handbook of Epilepsy Treatment, 3rd Edition, ISBN: 978-1-405-19818-9, December2010 p-132
52. Crawford PM, Managing epilepsy in women of childbearing age, Drug safety, 2009
53. Kaur J, Singh G, API-Medicine update, Chapter 83, Management of Epilepsy in Special Situations, 2017, p391-393
54. Hadi Manji, Seán Connolly, Neil Kitchen, Christian Lambert, and Amrish Mehta, Oxford hand book of neurology, 2nd edition,p458

55. Gooneratne I K, Wimalaratna M, Ranaweera A K P, Wimalaratna S. Contraception advice for women with epilepsy BMJ 2017; 357 :j2010 doi:10.1136/bmj.j2010.
56. Tomson T, Battino D, Bromley R, Kochen S, Meador K, Pennell P, Thomas SV. Management of epilepsy in pregnancy: a report from the International League Against Epilepsy Task Force on Women and Pregnancy. *Epileptic Disorders*. 2019 Dec;21(6):497-517.
57. Birnbaum AK, Meador KJ, Karanam A, Brown C, May RC, Gerard EE, Gedzelman ER, Penovich PE, Kalayjian LA, Cavitt J, Pack AM. Antiepileptic drug exposure in infants of breastfeeding mothers with epilepsy. *JAMA neurology*. 2020 Apr 1;77(4):441-50.
58. Kang, J.Y., Mintzer, S. Driving and Epilepsy: a Review of Important Issues. *Curr Neurol Neurosci Rep* 16, 80 (2016). <https://doi.org/10.1007/s11910-016-0677-y>.
59. Danielsson KC, Borthen I, Morken NH, Gilhus NE. Hypertensive pregnancy complications in women with epilepsy and antiepileptic drugs: a population-based cohort study of first pregnancies in Norway. *BMJ open*. 2018 Apr 1;8(4):e020998.
60. Giustozzi, M., Mazzetti, M., Paciaroni, M. et al. Concomitant Use of Direct Oral Anticoagulants and Antiepileptic Drugs: A Prospective Cohort Study in Patients with Atrial Fibrillation. *Clin Drug Investig* 41, 43–51 (2021). <https://doi.org/10.1007/s40261-020-00982-8>.
61. Zaccara G, Lattanzi S, Cincotta M, Russo E. Drug treatments in patients with cardiac diseases and epilepsy. *Acta Neurologica Scandinavica*. 2020 Jul;142(1):37-49.
62. Ladino LD, Téllez-Zenteno JF. Epilepsy and obesity: a complex interaction in the comorbidities of epilepsy 2019 Jan 1 (pp. 131-158). Academic Press.
63. Berg AT, Berkovic SF, Brodie MJ, Buchhalter J, Cross JH, van Emde Boas W, Engel J, French J, Glauser TA, Mathern GW, Moshé SL, Nordli D, Plouin P, Scheffer IE. Revised terminology and concepts for organization of seizures and epilepsies: report of the ILAE Commission on Classification and Terminology, 2005-2009. *Epilepsia*. [Internet] 2010 [cited on 2021 Feb 4]; 51(4):676-85. Available from: <https://pubmed.ncbi.nlm.nih.gov/> DOI: 10.1111/j.1528-1167.2010.02522.x.

64. Beghi E. Epilepsy syndromes in development. The concept of the epilepsy syndrome: How useful is it in clinical practice? *Epilepsia*. [Internet] 2009 [cited on 2021 Feb 4]; 50(Suppl. 5): 4–10. Available from: <https://onlinelibrary.wiley.com/doi/10.1111/j.1528-1167.2009.02112.x>.
65. Farrar MA, Park SB, Vucic S, Carey KA, Turner BJ, Gilling water TH, Swoboda KJ, Kiernan MC. Emerging therapies and challenges in spinal muscular atrophy. *Ann Neurol*. [Internet] 2017 [cited on 2021 Feb 4]; Mar;81(3):355-368. 419–429. Available from: <https://wileyonlinelibrary.com>. DOI: 10.1002/ana.24864.
66. Wheless JW, Pellock JM, Nordli DR, Sankar R. Pellock's Pediatric Epilepsy: Diagnosis and Therapy. 4th Edition, Demos Medical; 2016.
67. Epilepsia: Infantile Spasm: Metabolic work-up. *Epilepsia* 2010; 51:2175-2189.
68. Swaiman KF, Ashwal S, Ferriero DM, Schor NF, Finkel RS, Gropman AL, Pearl PL, Shevell M. Swaiman's Pediatric Neurology: Principles and Practice. 6th Edition. United Kingdom (UK): Elsevier Health Sciences, P-57,74,77.
69. Finbar J K O'Callaghan, Stuart W Edwards, Fabienne Dietrich Alber, Mario Cortina Borja, Eleanor Hancock, Anthony L Johnson et al. The Lancet Child & Adolescent Health, *Lancet Neurol*. 2005; 4: p -712–717.
70. Hussain SA. Treatment of infantile spasms. *Epilepsia Open* [Internet] 2018 [cited on 2021 Feb 4]; 3(s2):143–154. Available from: <https://onlinelibrary.wiley.com/doi/10.1002/epi4.12264>.
71. *Acta neurol: Dev Med & Child Neurol*. 53 (Suppl. 2): 2011. P - 1–6. v-vi .
72. Swaiman KF, Ashwal S, Ferriero DM, Schor NF, Finkel RS, Gropman AL, Pearl PL, Shevell M. Swaiman's Pediatric Neurology: Principles and Practice. 6th Edition. United Kingdom (UK): Elsevier Health Sciences, 2017; P-18-34.
73. Maryland, Kentucky, Utah. Utah medical drug report march 2019. Conversely, Figure 21. Field Division Reporting of. Controlled Prescription Drugs Availability in CY. 2018.
74. Jr. JE. A proposed diagnostic scheme for people with epileptic seizures and with epilepsy: report of the ILAE Task Force on Classification and Terminology. *Epilepsia Open* [Internet] 2001 [cited on 2021 Feb 4]; 42(6): 796-803. Available from: <https://onlinelibrary.wiley.com/DOI/10.1046/j.1528-1157.2001.10401.x>.

75. Kelley SA, Kossoff EH. Douse2 syndrome (myoclonic-astatic epilepsy): Developmental Medicine and Child Neurology. 2010 Nov;52(11):988-993.
76. Wier HA, Cerna A, So TY. Rufinamide for pediatric patients with Lennox-Gastaut syndrome: a comprehensive overview. Paediatr Drugs [Internet] 2011 [cited on 2021 Feb 4]; Apr 1;13(2):107-116. Available from: doi: 10.2165/11586920-000000000-00000.
77. Landau-Kleffner syndrome (LKS) and its LKS look-alikes. Epilepsia 1995;36 (Suppl. 4):13. Epilepsia 1992;33 (Suppl 3):122. Ho IK, Pediatrics 1999; 104:405–18.
78. Husain AM. New Features: An Update from the Journal of Clinical Neurophysiology, J Clin Neurophysiol [Internet] 2016 [cited on 2021 Feb 4]; Aug;33(4):299-300. Available from: <https://pubmed.ncbi.nlm.nih.gov/> doi: 10.1097/WNP.0000000000000324.
79. Swaiman KF, Ashwal S, Ferriero DM, Schor NF, Finkel RS, Gropman AL, Pearl PL, Shevell M. Swaiman's Pediatric Neurology: Principles and Practice. 6th Edition. United Kingdom (UK): Elsevier Health Sciences, 2017.
80. Linden ML, Hazlewood ME, Hillman SJ, Robb JE. Passive and dynamic rotation of the lower limbs in children with diplegic cerebral palsy. Dev Med Child Neurol [Internet] 2006 [cited on 2021 Feb 4]; Mar;48(3):176-80. Available from: <https://pubmed.ncbi.nlm.nih.gov/> doi: 10.1017/S0012162206000399.
81. Anne T. Berg. Recurrent Febrile Seizure. Febrile Seizure in Academic press; 2002: p 37-38.

[illegible]



SOCIETY OF NEUROLOGISTS OF BANGLADESH

Published by
Society of Neurologists of Bangladesh (SNB)
Website: <https://www.snb.org.bd/>
E-mail: snbdhaka2000@gmail.com