

## 1 Preamble

- 1.1 This guideline addresses the diagnosis and medical management of epilepsy in children, adults, and older people. It does not cover neonatal seizures or the management of febrile convulsions. The guideline may also be relevant to professionals working in the occupational health services, social services, educational services, or the voluntary sectors.
- 1.2 This guideline is evidence-based and the grading scheme used for the recommendations (**A, B, C, D**, good practice point [**GPP**]) is described in Appendix A.
- 1.3 This guideline represents consensus views of the Guideline Development Group and has been approved by the council of HKES. It is based on an appraisal of current scientific evidence and clinical information. It is not intended to cover all treatment modalities relevant to epilepsy, or to replace clinical judgement. The final treatment decision path should be reached by a formal discussion between individual patient and the treating physician.

## 2 Diagnosis, review, and referral

- 2.1 Diagnosis
  - All individuals with a recent-onset seizure should be seen urgently (ie being seen within 2 weeks) by a specialist (a specialist is defined as a medical practitioner with training and expertise in epilepsy) to ensure correct diagnosis and initiation of appropriate therapy.
  - The seizure type(s) and epilepsy syndrome, aetiology, and co-morbidity should be determined.
- 2.2 Review and referral
  - A comprehensive care plan should be agreed among health care professional, the individual with epilepsy, and their family or carers. All parties should participate in decisions about their health care, and take into account any specific needs.
  - All individuals with epilepsy should have a regular structured review. This review should be carried out at least yearly depending on how well the epilepsy is controlled and the presence of specific lifestyle issues.

## 3 Patient education

- 3.1 Individuals with epilepsy and their families or carers should be given information about: **C**
  - epilepsy in general
  - diagnosis and treatment options
  - medication and side-effects
  - seizure type(s), triggers and seizure control
  - risk management and self-care
  - first aid, safety and injury prevention at home/school/work
  - psychological issues
  - social services
  - education and health care at school
  - employment and independent living for adults
  - importance of disclosing epilepsy at work
  - home safety and driving
  - prognosis
  - sudden death in epilepsy
  - status epilepticus
  - lifestyle, leisure, and social issues (including recreational drugs, alcohol, sexual activity, and sleep deprivation)
  - family planning and pregnancy
  - voluntary organisations, eg support groups

Most of the above information is included in the booklet, *Your Guide to Epilepsy*, published by the HKES (4th edition, 2008).
- 3.2 The time at which this information is given will depend on the certainty of the diagnosis, and the need for confirmatory investigations. **GPP**
- 3.3 Adequate time should be given to provide information. Checklists may be used to remind both individuals and health care professionals about information that should be discussed during consultations. **GPP**

## 4 Following a first seizure

- 4.1 Urgency of evaluation
 

Hospital admission is recommended after the occurrence of a first convulsive seizure or in the presence of the following conditions: **D**

  - Fever or signs suggestive of infection
  - Prolonged seizure lasting more than 5 minutes
  - Cluster of seizures eg two or more seizures within 24 hours
  - Incomplete recovery after a seizure, eg drowsiness for more than 2 hours

- Persistent post-ictal focal neurological deficit

Advantages of hospital admission include:

- Prompt diagnostic evaluation looking for an important or treatable cause
- Close monitoring for possible emergence into status epilepticus
- Gathering important prognostic information for counselling

If hospital admission is considered unnecessary, a specialist appointment should be made within 2 weeks. **GPP**

#### 4.2 The initial evaluation

- A detailed history including a witness account and the circumstances at the time of seizure is necessary. **B**
- The differential diagnosis is wide (Appendix B1) and misdiagnosis is common.
- Preceding auras (eg epigastric rising sensation, auditory or visual hallucination, déjà vu) or Todd's paralysis are suggestive of partial seizure. **C**
- Limb stiffening, myoclonic jerks, jaw clenching, cyanosis, hypersalivation, head and neck version, and post-ictal confusion are features suggestive of generalised tonic-clonic seizure. **C**
- Physical examination during the post-ictal period is usually non-rewarding but certain clinical signs (eg lateral tongue biting, scald injury, posterior shoulder dislocation) would lend support to the diagnosis of epileptic seizure. **C**

#### 4.3 Classification of single seizures

Single seizures can be classified into two groups (A and B):

Group A: reactive or systemic causes

- Reactive seizures due to sleep deprivation, fever, drug withdrawal or toxicity
- Systemic diseases, eg infection, hypoglycaemia, hypoxia, hypocalcaemia

Group B: central nervous system insult or epilepsy

- Direct central nervous system insult, eg head injury, stroke, encephalitis, brain neoplasm
- First-seizure manifestation of symptomatic or idiopathic epilepsy

#### 4.4 The clinical importance of classification

- In Group A, seizures are usually self-limiting and recurrence may be reduced by correction of the provoking factor. In contrast, seizures in Group B are associated with subsequent recurrence and long-term AEDs may be necessary.

- Although AED may reduce the risk of seizures in reaction to head injury, craniotomy and cerebral malaria, such treatment does not affect the future development of epilepsy and hence routine prophylaxis is not indicated. **C**

#### 4.5 Biochemical and haematological tests

The following tests should be performed: **B**

- Complete blood cell count
- Urea, creatinine, electrolytes, calcium, glucose
- Liver function test, creatine kinase
- Urinalysis and toxicology screening (if indicated)

#### 4.6 Other investigations

- EEG performed within 24 hours of seizure has a higher probability of detecting epileptiform discharges than an EEG done on subsequent days. **B**
- CT/MRI of the brain is indicated to look for a structural brain lesion—CT brain is more appropriate in the emergency setting in association with bone fracture or haematoma, otherwise MRI brain is more sensitive. **C**
- Cerebrospinal fluid examination is indicated in the presence of fever and meningeal signs to establish the diagnosis of cerebral infection. **D**

#### 4.7 Emergency management after the first seizure

- In general, a single seizure usually self-terminates within 2 to 3 minutes and drug treatment may not be necessary. **D**
- Short-acting benzodiazepine (eg IV diazepam, diazemuls or midazolam) is indicated under the following circumstances to abort the onset of status epilepticus: **C**
  - (a) a convulsive attack lasting more than 2 minutes
  - (b) remaining drowsy in between attacks
  - (c) in the presence of a serious underlying cause, eg encephalitis, stroke
- See also the management of status epilepticus (Section 14)
- The underlying cause should be determined and specific treatment should commence as soon as possible (eg correction of biochemical abnormality, acyclovir for herpes encephalitis). **GPP**

#### 4.8 AED treatment after first seizure

- The initiation of AED treatment is determined by the risk of recurrence. **GPP**

- AED is not recommended in those with a normal workup as the cumulative risk of relapse in 2 years is less than 20%. **GPP**
  - The highest risk of recurrence occurs in those with both epileptiform EEG and a structural brain lesion (80-100%). An EEG with epileptiform discharges will increase the chance of recurrence from 20% to 80% (Appendix B2). **C**
  - Repeated standard EEGs may be helpful when the diagnosis of the epilepsy or the syndrome is unclear. However, if the diagnosis has been established, repeat EEGs are unlikely to be helpful in guiding response to treatment. **C**
  - When a standard EEG is non-rewarding, a sleep or sleep-deprived EEG should be performed. **C**
  - Long-term video/ambulatory EEG may establish diagnosis in difficult cases. Provocation by suggestion may be used in the evaluation of non-epileptic seizures. However, false-positive results may occur in some individuals. **C**
  - Photic stimulation and hyperventilation should remain part of standard EEG assessment unless contra-indicated (eg carotid stenosis). The individual and family and/or carer should be made aware that such activation procedures may induce a seizure and they have a right to refuse. **GPP**
- 4.9 General advice to patients after a first seizure
- The overall probability of developing a second seizure is about 42%.
  - The tendency of recurrence can be determined after a period of observation, eg 6 months to 2 years
  - To minimise the risk and impact of recurrence, advise the following: **GPP**
    - (a) Stop driving and inform the transport department
    - (b) Avoid operating dangerous machinery or work at height
    - (c) Restriction for at-risk hobbies, eg hiking, diving, and rock climbing
    - (d) Avoid sleep deprivation, recreational drugs, and alcohol
    - (e) Learn about the first-aid measures during a seizure

## 5 Investigations

### 5.1 EEG

- EEG is a useful test to confirm the diagnosis of epilepsy but it must be appropriately interpreted to avoid misdiagnosis. It should be performed within 4 weeks after it has been requested. **GPP**
- An EEG may be used to help determine seizure type and epilepsy syndrome which carry prognostic information. **C** Following a first unprovoked seizure, epileptiform discharges shown on EEG can be used to assess the risk of seizure recurrence (see Section 4.8). **B**
- A normal EEG should not be used to exclude epilepsy even though the clinical presentation supports the diagnosis of non-epileptic event. On the other hand, an abnormal EEG should not be used

### 5.2 Neuroimaging

- Neuroimaging should be used to identify structural abnormalities that cause certain epilepsies and MRI is the preferred mode of imaging. **C**
- MRI brain is particularly indicated in those: **C**
  - (a) with partial seizure onset based on history, examination, or EEG
  - (b) with seizures continuing in spite of first-line medication
- Neuroimaging should not be routinely requested when a diagnosis of idiopathic generalised epilepsy is firmly established. **C**
- CT brain should be used to identify underlying gross pathology if MRI is not available or is contra-indicated or in acute setting. **C**

### 5.3 Other tests

- Serum prolactin level is not recommended for diagnosis of epilepsy. **C**
- Other investigations, including blood and urine biochemistry, should be undertaken at the discretion of the specialist to exclude other diagnoses, to determine the underlying cause of the epilepsy and co-morbidity. **GPP**
- A 12-lead ECG should be performed with suspected epilepsy or diagnostic uncertainty. Referral to a cardiologist should be considered. **GPP**

- Genetic or metabolic causes of epilepsy should be considered and investigated in selected cases, eg muscle biopsy for mitochondrial disease, urine for uroporphyrinogen in suspected porphyria.

**GPP**

5.4 Neuropsychological assessment

- Neuropsychological assessment should be considered in individuals in whom it is important to evaluate learning disabilities and cognitive dysfunction, particularly in regard to language and memory. **D**
- Referral for a neuropsychological assessment should be considered: **D**
  - if there are educational or occupational difficulties
  - when MRI shows abnormalities in certain brain regions (eg temporal lobe)
  - when an individual complains of memory or other cognitive deficits
  - as part of presurgical evaluation

**6 Classification**

- Epileptic seizures and epilepsy syndromes in individuals should be classified using a multi-axial diagnostic scheme. The axes that should be considered are: description of seizure (ictal phenomenology); seizure type; syndrome and aetiology. Failure to classify the epilepsy syndrome correctly can lead to inappropriate treatment and persistence of seizures. **C**
- Individuals with epilepsy should be given information about their seizure type(s) and epilepsy syndrome, and the likely prognosis. **GPP**
- The ILAE diagnostic scheme (1981) divided the various seizures into partial-onset and generalised-onset. The former seizure type is further subdivided into simple and complex partial seizures and seizures evolving to secondarily generalised seizures. Classification of seizure type provides a guide to AED therapy (Appendix C1).
- The ILAE revised classification of the epilepsies and epileptic syndrome in 1989 has gained widespread acceptance among worldwide epileptologists (Appendix C2). It takes into account aetiological factors, age of onset, region of onset, and carries prognostic information. The choice of AED can be further refined based on the syndromic diagnosis (Appendix D2).

**7 Principles of management**

- A comprehensive care plan and counselling

TABLE 1. Factors affecting the choice of AEDs

AED-specific variable	Patient-specific variable	Nation-specific variable
Seizure or epilepsy syndrome	Genetic background	AED availability
Specific efficacy/effectiveness	Gender	AED cost
Dose-dependent adverse effects	Age	
Idiosyncratic reactions	Co-medications	
Chronic toxicities	Co-morbidities	
Teratogenicity	Insurance coverage	
Carcinogenicity	Relative wealth	
Pharmacokinetics	Ability to swallow pills/tablets	
Interaction potential		
Formulations		

on important issues (eg driving, schooling, employment, and pregnancy) should be discussed. **GPP**

- In newly diagnosed epilepsy, the aim of AED treatment is to achieve seizure freedom with minimal or no side-effect. In drug-resistant epilepsy, the treatment target would be achieving the best quality of life by striking a balance between AED efficacy and their associated side-effects. **GPP**

**8 Pharmacological or AED management**

- The AED treatment strategy should be individualised according to the seizure type and severity, epilepsy syndrome, co-medication and co-morbidity, the individual's lifestyle, characteristics, and preference (Table 1). **A**
- The initial choice of AED is guided by the seizure type or epilepsy syndrome (Appendices D and E). Because of lack of high-quality comparative studies among AED, only suggestions are made for each category. Other published guidelines (eg ILAE, American Academy of Neurology) may be consulted. **D**
- In general, patient factors should be matched with AED characteristics in terms of efficacy against seizure type/epilepsy syndrome, potential side-effects, teratogenicity, metabolism, and possible AED interactions. For instance, the side-effects of AED may be more apparent in certain patient groups and these may affect the choice of AED (Table 2). **GPP**
- Switching AED between different manufacturers is not recommended because of different bioavailability and pharmacokinetic profiles. Substitution may increase the potential for breakthrough seizures or excessive side-effects (Appendix D3). **GPP**

TABLE 2. Special considerations in different patient groups

Patient group	Considerations
Elderly	Impaired drug clearance and increased susceptibility to side-effect, eg hyponatremia due to carbamazepine; risk of polypharmacy and potential drug interactions
Children	Avoid phenobarbitone (behavioural disturbance) and phenytoin (cosmetic side-effect and erratic absorption)
Reproductive women	Avoid high-dose valproate (teratogenicity [see Section 16.5]), and avoid enzyme-inducing AEDs (carbamazepine, phenytoin, phenobarbital) if oral contraceptives are required
Cognitive dysfunction	Avoid phenobarbitone, benzodiazepines and topiramate if risk of cognitive slowing is unacceptable
Mitochondrial diseases	Avoid valproate
Advanced renal failure	Reduce dose of AEDs that are primarily excreted by renal route, eg gabapentin, pregabalin
Active liver disease	Avoid valproate (risk of hepatic encephalopathy)
Eating disorders	Avoid topiramate
Morbid obesity	Avoid valproate, pregabalin

8.5 Single AED (monotherapy) treatment is preferred to polytherapy wherever possible. **A** If the first AED is unsuccessful, another monotherapy may be started and built up to an adequate dose before the first AED is tapered off slowly. **GPP**

8.6 If the second drug is unhelpful, either the first or second drug may be tapered, depending on their relative efficacy and side-effects. **GPP**

8.7 Combination (adjunctive or 'add-on') therapy should be considered if monotherapy trials fail to control the epilepsy. **A**

8.8 Beware of drug-drug interactions among AEDs and between AEDs and non-AEDs, eg warfarin, oral contraceptive pills via effects of AED on hepatic cytochrome P450 enzyme system. Carbamazepine, phenobarbital, phenytoin are broad enzyme inducers with many interactions including oral contraceptive pills. Oxcarbazepine and topiramate (>200 mg per day) induce metabolism of oral contraceptive pills. Gabapentin and pregabalin (both excreted renally unchanged), and levetiracetam (non-hepatic hydrolysis) have lowest potential of drug-drug interactions. **A**

8.9 Valproate significantly inhibits the metabolism of lamotrigine. When lamotrigine is added to a drug regimen containing valproate, it should be titrated more slowly to reach a lower maintenance dose. **A** This practice may reduce the incidence of dose-dependent adverse effects of lamotrigine, particularly skin rash. **B**

8.10 Regular blood tests for 'routine' haematological and renal and liver functions are not necessary and should be done only if clinically indicated. Asymptomatic minor laboratory abnormalities do not necessarily require changes in medication. **C**

8.11 Routine monitoring of serum AED level is not

indicated. Specific indications for monitoring of serum AED levels include: **D**

- suspected AED toxicity
- detection of non-compliance to the prescribed AED
- adjustment of phenytoin dose
- management of pharmacokinetic interactions
- specific conditions, eg status epilepticus, organ failure, and pregnancy

### Withdrawal of pharmacological treatment

8.12 For adults who have been seizure-free for 2 years or more, the decision to continue or withdraw AED should be taken by the individual and the specialist after a full discussion of the risks and benefits of withdrawal. **A** (see Sections 18.1 to 18.13).

8.13 AED treatment should be discontinued slowly with one drug being withdrawn at a time. **D** A more prolonged time course (up to 6 months) is required for withdrawing benzodiazepines and barbiturate to avoid withdrawal symptoms and seizure recurrence. If seizure recurs, the last dose reduction is reversed and medical advice is sought. **GPP**

## 9 Management of drug-resistant epilepsy

9.1 About 70% of people with newly diagnosed epilepsy respond well to AED. Drug-resistant epilepsy may be operationally defined as persistence of seizures despite optimal and adequate treatment trials with two AEDs (either monotherapy or polytherapy) appropriately chosen for the seizure type/epilepsy syndrome. **D**

9.2 In people with drug-resistant epilepsy,



consideration should be given to the possibility of 'pseudo-resistance', referring to treatment failure due to: **C**

- incorrect diagnosis of epilepsy
- inappropriate choice of AED for the seizure type/epilepsy syndrome
- inadequate dosage of AED
- poor compliance to treatment
- unsatisfactory lifestyle such as drug or alcohol abuse

- 9.3 People fulfilling a diagnosis of drug-resistant epilepsy should undergo, preferably at a specialist centre, comprehensive evaluation of the diagnosis and management, which may include workup for epilepsy surgery. **C**

## 10 Side-effects of AEDs (Appendix D4)

### Dose-related adverse reactions

- 10.1 Neurotoxic side-effects (eg dizziness, somnolence, diplopia, ataxia) are mostly dose-related and predictable. These can be reduced by gradual escalation of dose and dose reduction if symptoms persist. **A**

### Idiosyncratic drug reactions

- 10.2 Idiosyncratic drug reactions usually occur in the first few weeks of treatment and are potentially serious. Skin rash is the most common, occurring in up to 10% of patients on carbamazepine, lamotrigine, oxcarbazepine, phenobarbital, and phenytoin. Cross hypersensitivity is common. Most rashes are mild and resolve promptly on discontinuation of the AED, but severe cutaneous reactions (Stevens-Johnson syndrome and toxic epidermal necrolysis) are seen in up to 1:1000 patients.
- 10.3 HLA-B\*1502 allele (present in 10-20% Chinese in Hong Kong) is associated with a dramatically increased risk of carbamazepine-induced severe cutaneous reactions in people with susceptible ethnic backgrounds, eg Han Chinese. Prior to starting carbamazepine, people who are ethnically Chinese should be tested for HLA-B\*1502. Carbamazepine should be avoided if the test is positive unless the benefits from treatment outweigh the risk of developing severe cutaneous reactions (see FDA Alert: Information for healthcare professionals: carbamazepine <[www.ifap.de/pdf/FDA\\_carbamazepin-warning\\_2007-12-12.pdf](http://www.ifap.de/pdf/FDA_carbamazepin-warning_2007-12-12.pdf)>).
- 10.4 AED hypersensitivity syndrome of fever, rash, lymphadenopathy, and multi-organ failure occurs in up to 4:10 000 patients, mostly with aromatic AEDs (carbamazepine, phenytoin, phenobarbital) or lamotrigine. Cross-sensitivity

may occur between aromatic AEDs in up to 50% of patients. **B**

- 10.5 Minor blood dyscrasias are associated with many AEDs, eg leukopenia with carbamazepine, thrombocytopenia with valproate. **GPP**
- 10.6 Hyponatremia (sodium 125-135 mmol/L) is seen in about 20% of patients taking carbamazepine or oxcarbazepine, which is usually asymptomatic. Mild elevation of liver enzymes (gamma GTP or alkaline phosphatase) is commonly seen in people taking enzyme-inducing AEDs. **GPP**

### Chronic side-effects

- 10.7 Vigabatrin should be used as drug of last choice (except infantile spasm) because of its association with high incidence of visual field defects. **B**
- 10.8 Weight gain is seen with many AEDs (eg valproate, gabapentin, pregabalin) and may be significant (>10% body weight). In contrast, topiramate can cause weight loss. **B**
- 10.9 People with epilepsy taking long-term AED are prone to have osteoporosis, osteomalacia, and fractures. Cytochrome P450 enzyme-inducing AEDs are most commonly associated with a negative impact on bone, but studies also suggest an effect of valproate. There are limited data regarding the newer AED. They are advised to have adequate intake of dietary calcium and vitamin D together with regular bone density monitoring. **D**
- 10.10 Teratogenicity of AED is discussed in Section 16.
- 10.11 Certain AED may exacerbate some seizure types and epilepsy syndromes and should be avoided accordingly (Appendix D1 and D2).

## 11 Presurgical evaluation of drug-resistant epilepsy

- 11.1 A comprehensive presurgical evaluation entails a multidisciplinary team of experts (neurologists, paediatricians specialising in neurology/epilepsy, neurosurgeons, neuro-radiologists, psychiatrists, and clinical psychologists). Multi-modal investigations may be undertaken including video-EEG recording, CT, MRI, functional MRI, PET, SPECT, MEG, angiogram and intracarotid amobarbital test, intracranial EEG monitoring, and functional mapping to evaluate brain function.

### Referrals for presurgical evaluation

- 11.2 If there is diagnostic uncertainty or treatment failure, individuals should be referred to tertiary

services for further assessment.

Indications for referral include the following: **D**

- drug-resistant epilepsy
- the individual is aged under 2 years
- unacceptable side-effects from medication
- there is a unilateral structural lesion
- there is psychological and/or psychiatric co-morbidity
- there is diagnostic doubt as to the nature of the seizures
- there is a testable hypothesis for localising the epileptogenic zone

11.3 Different scenarios determine complexity of investigations:

*Scenario 1:* a focal lesion on MRI with concordant scalp EEG and congruent results of functional evaluation. The classical prototype is a right-handed individual with right mesial temporal sclerosis, ictal right temporal EEG onset, interictal right temporal EEG discharges, clinical psychological testing showing impaired figurative memory and normal verbal memory.

**A**

*Scenario 2:* focal or multiple lesions on MRI with or without discordant scalp EEG or incongruent results of functional evaluation. This entails a heterogeneous group of patients with discordant results. Multi-modal investigations and multidisciplinary discussions are usually undertaken and there may be a need for intracranial implantation to localise the epileptogenic zones. Individualised approach is usually adopted. **C**

*Scenario 3:* resection close to eloquent areas. Consideration should be given to functional mapping, which may be undertaken intra-operatively or extra-operatively with grid implantation. Extra-operative functional mapping may provide more sophisticated testing of brain functions. **C**

*Scenario 4:* non-lesional or 'cryptogenic' cases. Investigations are necessary to rule out idiopathic generalised epilepsy. Multi-modal investigations and intracranial implantation will be required in the majority of cases. **C**

*Scenario 5:* resective surgery not applicable. Palliative neurosurgery, eg corpus callosotomy or vagus nerve stimulation, may be considered. **C**

### Special considerations in paediatric epilepsy surgery

11.4 The spectrum of localisation-related epilepsy is often heterogeneous in childhood and may present with generalised seizures or EEG

patterns, as well as progressive neurological dysfunction. **C**

11.5 Unclassifiable childhood epilepsy should be referred for presurgical evaluation, eg non-idiopathic partial seizures or lesional epilepsy. **D**

11.6 Age-appropriate neuropsychological and developmental assessments are mandatory in those with developmental delay but such impairment should not exclude them from epilepsy surgery. **D**

11.7 Epilepsy surgery consists of cortical resection or disconnection procedures. Surgical remediable syndromes were more diverse in children, including mesial temporal sclerosis, cortical dysplasia, developmental brain anomalies and tumour, tuberous sclerosis, Rasmussen's encephalitis, hypothalamic hamartoma, and vascular malformations. **D**

11.8 Functional plasticity in the child's brain could enhance the recovery of linguistic competence and facilitate neurological re-organisation after surgical treatment. Early intervention is therefore critical in infants with catastrophic epilepsy to prevent developmental arrest or regression. **C**

11.9 Corpus callosotomy is a palliative epilepsy surgery to block interhemispheric spread of secondarily generalised seizures. Corpus callosotomy is especially effective for tonic and atonic seizures causing falls and consequent injuries, eg Lennox-Gastaut syndrome. **C**

## 12 Other forms of treatment

### Psychological interventions

12.1 Psychological interventions (relaxation, cognitive behaviour therapy, biofeedback) may be used in conjunction with AED in adults. This approach may be associated with an improved quality of life in some individuals. **A**

12.2 Psychological therapy has not been proven to affect seizure frequency and is not an alternative to AED treatment. **A**

### Ketogenic diet

12.3 The ketogenic may be considered an adjunctive treatment in children with drug-resistant epilepsy. The responder rate (more than 50% seizure reduction) is close to 40%. **A** Side-effects include constipation, vomiting, lethargy, hunger, acidosis, easy bruising, and nephrolithiasis. Contra-indications include those with fat metabolic disorders and porphyria.

TABLE 3. Guideline for treating convulsive status epilepticus

General measures	Pharmacological treatment
<p>Premonitory status (prehospital)</p> <ul style="list-style-type: none"> <li>• Out-of-hospital management for acute seizure</li> <li>• Common sense to prevent injuries, eg cushion the person's head, loosen any tight neckwear, turn the person on his or her side</li> <li>• Do not hold the person down or restrain the person</li> <li>• Do not place anything in the mouth</li> <li>• Do not try to pry the teeth apart</li> <li>• Observe seizure characteristics—length, type of movements, direction of head or eye turning</li> </ul>	<ol style="list-style-type: none"> <li>1. Rectal diazepam 10-20 mg, repeated once 15 minutes later if seizure continues, OR</li> <li>2. Buccal midazolam 10 mg</li> </ol> <p>If seizures continue, call emergency ambulance service and continue anticonvulsant as below.</p>
<p>Early status I (0-10 minutes)</p> <ul style="list-style-type: none"> <li>• Resuscitation, secure airway (consider intubation), administer oxygen, assess cardiorespiratory function and establish IV access, haemoglucofix</li> </ul> <p>Early status II (0-30 minutes)</p> <ul style="list-style-type: none"> <li>• Institute regular monitoring, emergency investigations</li> <li>• Administer glucose (50 mL of 50% solution) and/or IV thiamine (250 mg)</li> <li>• Treat acidosis if severe</li> <li>• Consider the possibility of non-epileptic status</li> </ul>	<ol style="list-style-type: none"> <li>1. Lorazepam IV 0.1 mg/kg (usually 2-4 mg bolus, repeated once after 10-20 minutes) OR</li> <li>2. Diazepam IV 0.1 mg/kg (usually IV 5-10 mg bolus, repeated once after 5-10 minutes) OR</li> <li>3. If already on AED, resume usual medication</li> </ol> <p>For sustained control or if seizures continue, treat as below.</p>
<p>Established status (0-60 minutes)</p> <ul style="list-style-type: none"> <li>• To establish aetiology</li> <li>• Arrange ICU bed</li> <li>• Identify and treat complications, including use of vasopressor, if appropriate</li> </ul>	<ol style="list-style-type: none"> <li>1. Phenytoin infusion at a dose of 15-18 mg/kg at a rate of 50 mg/minute OR</li> <li>2. Fosphenytoin infusion at a dose of 15-20 mg phenytoin equivalents (PE) per kg at a rate of 50-150 mg PE/minute AND/OR</li> <li>3. phenobarbitone bolus of 10-15 mg/kg at a rate of 100 mg/minute</li> </ol>
<p>Refractory status (30-90 minutes)</p> <ul style="list-style-type: none"> <li>• Transfer to ICU, and EEG monitoring</li> <li>• Consider the possibility of non-epileptic status</li> <li>• Intracranial pressure monitoring, if appropriate</li> <li>• Initiate long-term, maintenance AED therapy</li> </ul>	<p>General anaesthesia, with one of the following:</p> <ol style="list-style-type: none"> <li>a. propofol (1-2 mg/kg bolus, then 2-10 mg/kg/hour)</li> <li>b. midazolam (0.1-0.2 mg/kg bolus, then 0.05-0.5 mg/kg/hour)</li> <li>c. thiopentone (3-5 mg/kg bolus, then 3-5 mg/kg/hour) [after 2-3 days infusion rate needs reduction as fat stores are saturated]</li> </ol> <p>Anaesthetic continued for 12-24 hours after the last clinical or electrographic seizure, then dose tapered.</p>

12.4 The modified Atkins diet (restricting carbohydrate intake to 10 g in children and 15 g in adults) has a 45% responder rate. **C**

### Vagus nerve stimulation

12.5 Vagus nerve stimulation is indicated as an adjunctive therapy in reducing the frequency of seizures in drug-resistant epilepsy not amenable to surgery. The efficacy of vagus nerve stimulation is similar to that obtained with new AEDs. **A** Side-effects are usually mild, eg cough and transient hoarseness of voice.

### Gamma knife radiosurgery

12.6 Gamma knife radio surgery may be effective in patients with mesial temporal sclerosis but a delayed response by 10 months is observed. The long-term side-effects are unknown. It is also effective in treating focal epilepsy due to cavernous angiomas in central region and gelastic seizures in hypothalamic hamartomas. **C**

## 13 Prolonged seizures in the community

13.1 An individual who has prolonged convulsive

seizures (lasting 5 minutes or more) or serial seizures (three or more seizures in an hour) in the community should receive urgent care and treatment. **A**

13.2 Rectal diazepam is a safe and effective first-line treatment of prolonged seizures. **A** Buccal midazolam is an alternative which is easier to be administered and considered more acceptable for patients and administrators. **C**

## 14 Treatment of status epilepticus

14.1 Convulsive status epilepticus is a medical emergency.

- General measures include airway management, setting up IV access, oxygen supplement, cardiorespiratory function monitoring. **GPP**
- IV lorazepam is a first-line treatment in status epilepticus and alternatives include IV diazepam, diazepam, and midazolam. **D** These can be repeated if necessary. Close monitoring of cardiorespiratory function is mandatory.
- Full blood count, urea, and electrolytes, liver function tests, blood gases, calcium, glucose, clotting profile and AED level(s)



TABLE 4. Alternative methods of AED administration

AED	Alternative administration
Carbamazepine	Liquid or suppositories (dose amendment required)
Phenytoin	IV or liquid phenytoin; IV or IM fosphenytoin
Gabapentin	Capsule contents via feeding tube (unlicensed)
Levetiracetam	Liquid or IV
Lamotrigine	Dispersible tablets can be given via feeding tube
Valproate	IV, liquid, or suppositories (unlicensed)
Topiramate	Sprinkle capsules
Vigabatrin	Powder
Phenobarbital	Liquid; IV or IM injection

are indicated. **C**

- Give 50 mL of 50% glucose IV for hypoglycaemia and IV thiamine if alcohol abuse or poor nutritional status is suspected. **C**
- For patients with epilepsy, the usual AED shall be resumed with dosage adjustment if necessary. Otherwise a loading dose of AED should be given (Table 3). **B** The rate of AED infusion may need to be adjusted if hypotension or arrhythmia occurs. In selected cases, IV valproate or levetiracetam may be used. **D**
- If seizure continues, ICU admission is indicated for administration of anaesthetic agent (Table 3), EEG monitoring and critical life support. The cause of status epilepticus shall be investigated and treated. **C**

14.2 Non-convulsive status epilepticus is less common. Continuation of usual AED and IV benzodiazepines with EEG monitoring are useful. **GPP**

## 15 Perioperative management of seizure

15.1 Loss of seizure control due to missed oral AED can occur during surgery, labour and when there is difficulty in swallowing. Table 4 lists some alternative routes of AED administration. Sometimes changes in drug doses will be necessary due to pharmacokinetic differences between formulations. **C**

15.2 AEDs should be administered by alternative routes or by giving additional doses as appropriate. When patients have been designated nil by mouth prior to surgery, they should still be given their usual oral AED unless absorption is impaired. **GPP**

15.3 When a prolonged problem with administered

drugs not available parenterally is anticipated, and oral or enteral administration is not possible, consideration should be given to seizure prophylaxis with parenterally available agents. **GPP**

## 16 Women with epilepsy

16.1 Women with epilepsy and their spouses should receive information and counselling on contraception, conception, pregnancy, child-care, breastfeeding, and menopause. **C**

16.2 Preconception counselling should be given to women of childbearing age with epilepsy. They should be reassured that most can have an uneventful pregnancy and delivery. **GPP**

16.3 In women of childbearing potential, the risk of AEDs causing harm to foetus should be adequately discussed. The treatment strategy should be targeted at the lowest effective dose of the most appropriate AED. Monotherapy is preferred to polytherapy. **C**

### Teratogenicity of AEDs

16.4 Common associated major congenital anomalies consist of hypospadias, heart defects, club foot, cleft lip or palate. These occur in the general population at a rate of 2 to 5%. The risk of such major congenital anomalies is increased to 4 to 10% in infants exposed to the old AEDs especially for those who are receiving AED polytherapy. **C**

16.5 Neural tube defects occur in 1 to 2.2% with carbamazepine but a dose-escalating risk has been observed with both valproate and lamotrigine: 4.1% with valproate at <600 mg/day; 1.3% with lamotrigine <100 mg/day, 6% with valproate 600-1000 mg/day, 1.9% with lamotrigine at 100-200 mg/day, 9.1% with valproate at >1000 mg/day, 5.4% with lamotrigine >200 mg/day. **C** Screening of neural tube defects by ultrasound and alpha-fetoprotein should be carried out at 18 to 22 weeks' gestation. **GPP**

16.6 In-utero exposure to high-dose valproate is associated with an increased risk of impaired cognitive function at 3 years of age. This finding supports a recommendation that other alternatives should be considered as first-choice therapy in women of childbearing potential. **C**

16.7 There are insufficient data to evaluate the teratogenicity potential among other newer AEDs, eg topiramate, levetiracetam, and gabapentin.

16.8 Daily folate (5 mg) supplement should be given before pregnancy. **D**

## Contraception

- 16.9 AED interaction with oral contraceptive pills should be discussed. **GPP**
- 16.10 If a woman taking enzyme-inducing AEDs (carbamazepine, oxcarbazepine, phenobarbital, phenytoin, primidone, topiramate) requires hormonal contraception, the following regimens are recommended:
- For combined oral contraceptive pills, a minimum initial dose of 50 µg of oestrogen should be commenced. **D**
  - If breakthrough bleeding occurs, the dose of oestrogen should be increased to 75 or 100 µg per day, and 'tricycling' (taking three packs without a break) should be considered. **D**
  - A shorter repeat injection interval is recommended (10 weeks rather than 12 weeks) for depot injections of progesterone (eg Depo-Provera 150 mg) **D**
  - For emergency contraception, the dose of levonorgestrel should be increased to 1.5 mg and 750 µg with 12 hours apart. **D**

## Pregnancy

- 16.11 Women should be reassured that there is no evidence that simple partial, complex partial, absence and myoclonic seizures affect the pregnancy or developing foetus adversely unless they fall and sustain an injury. **D**
- 16.12 Sixty percent of women experience no change in frequency during pregnancy, 30% increased frequency and 10% decreased frequency. The increase in seizure frequency may be due to pregnancy-related fall in AED concentration, sleep deprivation, or poor compliance. **B**
- 16.13 Routine monitoring of most AED levels in pregnancy is not necessary. However, this may be used to guide dosage adjustment should seizure frequency increase. **D**
- 16.14 Both total and free clearance of lamotrigine may increase substantially during pregnancy with peak at the third trimester (up to 90-230%). A drop of lamotrigine level to 65% of the preconceptional level is associated with an increase in seizure frequency. **A** Monitoring of lamotrigine level, if available, is useful to adjust dosage of lamotrigine during pregnancy.

## Labour

- 16.15 About 1 to 2% of women with epilepsy develop a generalised tonic-clonic seizure during labour. AEDs should be continued orally or via IV route if necessary. Epidural anaesthesia is

recommended to reduce pain and emotional distress. Elective caesarean section may be necessary if seizures are frequent. **D**

- 16.16 To prevent haemorrhagic disease of newborn, mothers taking enzyme-inducing AEDs may be given 20 mg/day of oral vitamin K1 in the last month of pregnancy. Alternatively, their newborns should be given 1 mg of vitamin K<sub>1</sub> parenterally at delivery. **C**

## Breastfeeding and the puerperium

- 16.17 All women with epilepsy should be encouraged to breastfeed, which is safe in the majority of cases. **GPP** As most AEDs are secreted in breast milk in small quantities, the infant may become sedated (in about 5-10%). Under these circumstances, bottle-feeding can be used to supplement breastfeeding.
- 16.18 Mothers should breastfeed their babies while sitting on floor cushions to avoid dropping their baby should a seizure occur. Bathing the babies in the bathtub is not recommended. **GPP**

## Menopause

- 16.19 Clinician must remind patients that hormonal replacement therapy is significantly associated with increase in seizure frequency during menopause, particularly in women with history of catamenial epilepsy. **C**

## 17 Older people with epilepsy

- 17.1 Generalised convulsions and complex partial seizures (mainly extra-temporal) are the main clinical manifestations of epilepsy in the elderly. The latter may present with staring, blackouts, or dizziness which may be mistaken as transient ischaemic attack or syncope.
- 17.2 In view of the altered pharmacokinetics and pharmacodynamics in the elderly, side-effects of most AEDs are more apparent and a lower starting dosage is recommended. Drug interactions may constitute a significant problem because of polytherapy associated with co-morbidities. The newer AED, eg gabapentin, lamotrigine are shown to be better tolerated in the elderly with similar efficacy compared with the old AEDs. **B**

## 18 Children and young people with epilepsy

### After first seizure

- 18.1 'Airway, breathing and circulation' should be preserved according to established paediatric life support guideline. If the child shows full

recovery after the first seizure, it is not necessary to check full blood count or electrolytes unless there are specific features on history and examination to suggest this might be helpful.

### Differential diagnosis

18.2 Misdiagnosis of epilepsy appears to be a significant problem and may have major longer-term implications (Appendix B3). The diagnosis of epilepsy should be made by a paediatric neurologist or paediatrician with expertise in childhood epilepsy. **D** Home video camera recordings should be used in order to capture recurrent events where the diagnosis is in doubt. **GPP**

### Investigations

18.3 Investigations

- All children presenting with convulsive seizures should have an ECG with a calculation of the QTc interval, in order to rule out epileptic or epileptic events associated with cardiogenic syncope. **GPP**
- All children with recurrent epileptic seizures other than recurrent or complex febrile seizures should have an EEG. **C** AEDs should not usually be started before an EEG recording since it may mask a syndromic diagnosis. **GPP**
- Most children with epilepsy should have an elective MRI brain scan. Children with the following epilepsy syndromes (which follow a typical course) do not need brain imaging—eg idiopathic generalised epilepsies (childhood absence epilepsy, juvenile myoclonic epilepsy, juvenile absence epilepsy etc); benign childhood epilepsy with centrotemporal spikes. **D**

### Genetic testing

18.4 Where one person in a family has idiopathic epilepsy, the recurrence risk for siblings is 2.5 to 6.7% and for children is 1.6 to 6.3%. The recurrence risk for symptomatic epilepsies relates to the underlying aetiology. In all patients with newly diagnosed epilepsy, a three-generation family history should be taken (ie siblings, parents and grandparents, uncles, aunts, cousins). Families with a history of epilepsy should be referred to the Clinical Genetic Service particularly if three or more members of the family are affected. **GPP**

### Pyridoxine dependency

18.5 Pyridoxine-dependent seizures form a rare,

but easily treatable epilepsy syndrome where seizures are largely resistant to AED. While there are typical neonatal presentations, children may present up until the third year of life. A trial of pyridoxine and its withdrawal is needed to diagnose pyridoxine dependency and should be considered in children with intractable epilepsy with onset under the age of 3 years. **GPP**

### Febrile seizures

18.6 Children with febrile seizures, even if recurrent, should not be treated prophylactically with AED. **B** For details, please refer to the following website: <<http://www.fmskhk.org/hkcpaed/member/guideline/fc.pdf>>

### Choice of AEDs (Appendices D and E)

18.7 When West's syndrome is caused by tuberous sclerosis, vigabatrin is superior. For other aetiologies and cryptogenic forms of West's syndrome, corticotrophin or corticosteroids should be used as first-line treatment. **B**

18.8 In drug-resistant idiopathic generalised epilepsy, topiramate, lamotrigine, levetiracetam and clobazam are effective as add-on treatments. Lamotrigine, topiramate and nitrazepam are effective add-on treatments in Lennox-Gastaut syndrome. Stiripentol has antiepileptic activity in Dravet's syndrome when used with clobazam and sodium valproate. High-dose valproate, nitrazepam and topiramate are efficacious in resistant West's syndrome. **B**

18.9 Prolonged or serial seizures should be treated with either nasal or buccal midazolam or rectal diazepam. **B** All units admitting children should have a protocol for the management of convulsive status epilepticus. **GPP**

18.10 Clear advice on the management of the potential adverse effects of AED should be discussed with children and parents or carers. Adolescent girls taking AED and their parents should be advised of the risks of foetal malformations and developmental delay (see Section 16). **GPP**

### Withdrawal of AED treatment

18.11 AED withdrawal should be considered in children who have been seizure-free for 2 or more years. Reasons for withdrawal include:

- concern about side-effects of AED
- avoid teratogenic side-effects on the foetus
- psychological gratification, eg feeling cured, removal of stigmata

18.12 Risk factors for seizure relapse include

symptomatic epilepsy, more than 12 years of age at seizure onset, short duration of seizure freedom (less than 6 months), an abnormal EEG at discontinuation and certain syndromal diagnosis, such as juvenile myoclonic epilepsy.

**A**

- 18.13 If seizure recurs, it usually occurs shortly after AED withdrawal. The risk of relapse is about 30% in children and 40% in adults. Seizure control may not be regained in up to 20% after relapse. These risks have to be balanced with the potential gain and the final decision should be individualised. **GPP**

### Behaviour and learning

- 18.14 Learning and behavioural problems are more prevalent in children with epilepsy than in the general childhood population. All children with epilepsy should have their behavioural and academic progress reviewed on a regular basis by the epilepsy team. Children with academic or behavioural difficulties should have appropriate educational and/or psychological assessment and intervention. **GPP**

### Use of other medications

- 18.15 Neurostimulants should not be withheld, when indicated, from children with epilepsy and attention deficit and hyperactivity disorders. **D**
- 18.16 Selective serotonin reuptake inhibitors and atypical neuroleptics such as risperidone should not be withheld, when indicated, in children with epilepsy and associated behavioural and psychiatric disorders. **GPP**

### Transitional care

- 18.17 During adolescence, smooth transition of care to adult services and the possible need for continuing multi-agency support should be considered. **GPP**
- 18.18 Adolescents may be stressed by restriction of recreational activities. They are concerned about side-effects of AEDs (eg weight gain) and may feel inferior to their peer group. Psychological counselling is essential. **GPP**

## 19 Lifestyle and social issues

### Advice on minimising hazards at home

- 19.1 Clinicians should give advice on minimising possible hazards at home in case seizures happen (eg use shower rather than bathtub). **D**

### Hazards at work

- 19.2 Advice should be given on suitability of particular job to people with epilepsy taking into account the job requirements and seizure characteristics. **D**

### Sports and leisure activities

- 19.3 People with epilepsy are recommended to have appropriate sports for health and social well-being. Epilepsy is not a reason to prohibit them from sports (even competitive types), provided adequate safety measures have been taken. **D**
- 19.4 Seizure risk is higher during relaxation period after sport as compared to during sport-playing. **D**
- 19.5 Either swimming alone or diving is hazardous. Accompanying person with lifesaving skills is essential. **D**

### Driving and epilepsy

- 19.6 Since seizures may result in losing control of the vehicle leading to road traffic accidents, people with epilepsy are legally prohibited to drive in Hong Kong.
- 19.7 People with epilepsy are obliged to notify the Transport Department regarding their medical diagnosis.
- 19.8 An individual with inactive epilepsy may apply for a driving licence under special circumstances but the outcome is subject to approval by the Transport Department.
- 19.9 Driving is considered a privilege, not a right. Use of public transport is recommended for people with epilepsy.
- 19.10 Certain occupations are restricted for people with epilepsy, eg drivers for public transport, pilots, operators of heavy machinery, eg cranes, tractors.

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# Appendices

## Appendix A. Grading scheme of evidence

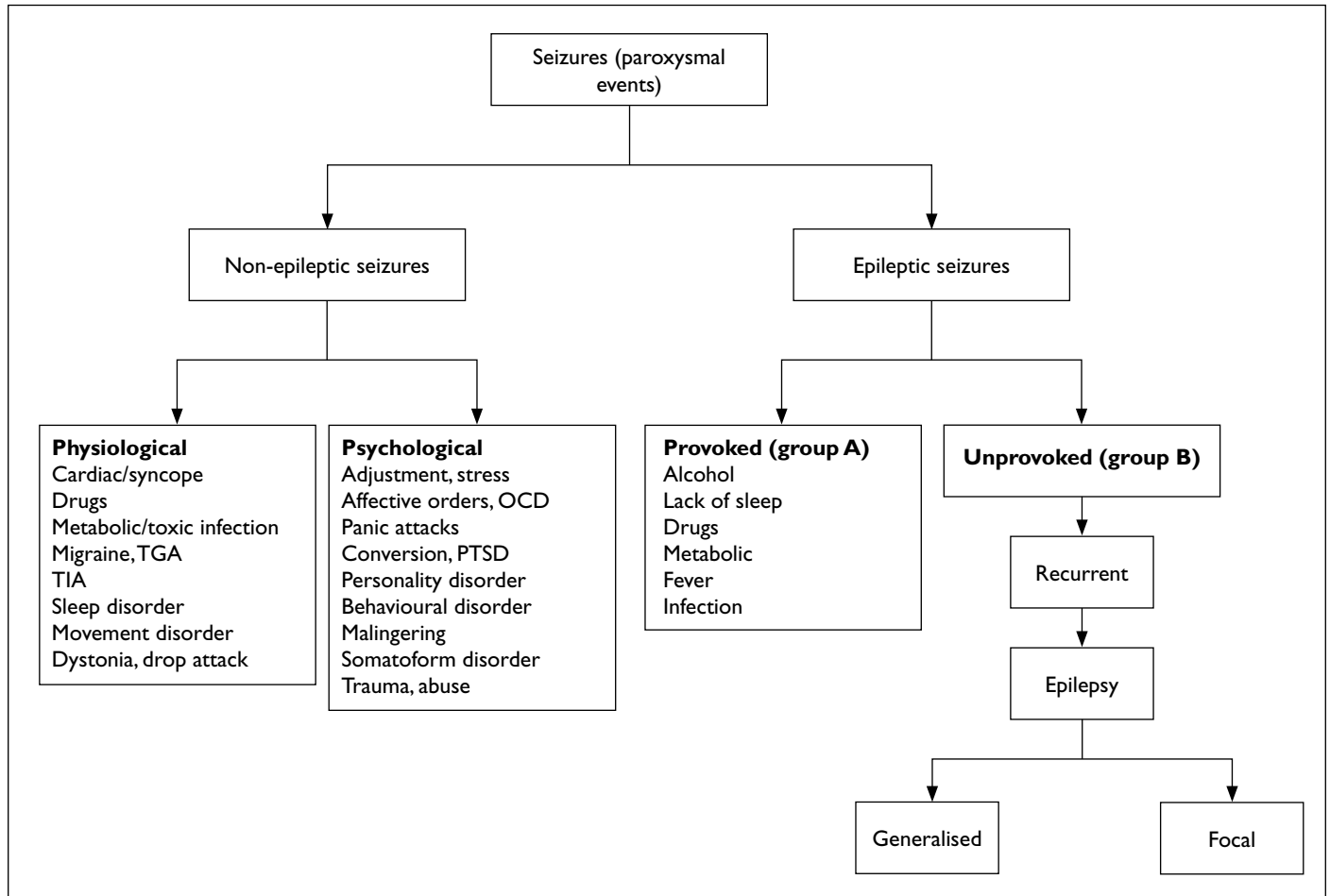
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Recommendation grade	Evidence
A	Directly based on category I evidence
B	Directly based on: <ul style="list-style-type: none"><li>• category II evidence, or</li><li>• extrapolated recommendation from category I evidence</li></ul>
C	Directly based on: <ul style="list-style-type: none"><li>• category III evidence, or</li><li>• extrapolated recommendation from category I or II evidence</li></ul>
D	Directly based on: <ul style="list-style-type: none"><li>• category IV evidence, or</li><li>• extrapolated recommendation from category I,II or III evidence</li></ul>
GPP	Good practice point based on the clinical experience of the Guideline Development Group
Evidence category	Source
I	Evidence from: <ul style="list-style-type: none"><li>• meta-analysis of randomised controlled trials, or at least one randomised controlled trial</li></ul>
II	Evidence from: <ul style="list-style-type: none"><li>• at least one controlled study without randomisation, or</li><li>• at least one other type of quasi-experimental study</li></ul>
III	Evidence from non-experimental descriptive studies, such as comparative studies, correlation studies, and case-control studies
IV	Evidence from expert committee reports or opinions and/or clinical experience of respected authorities

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## Appendix B. Differential diagnosis of epileptic seizures and epileptiform discharges

### Appendix B1. Differential diagnosis of epilepsy in adults



TGA denotes transient global amnesia, TIA transient ischaemic attack, OCD obsessive compulsive disorder, and PTSD post-traumatic stress disorder

### Appendix B2. Differential diagnosis of epileptiform discharges

Interictal epileptiform discharges	Benign EEG variants and sleep transients	Common EEG artifacts
Spikes	Small sharp spikes	Eye movement
Spikes and slow waves	Occipital spikes of the blind	Electrocardiogram
Sharp waves	14 and 6 Hz positive spike	Head movement
Sharp and slow waves	Rhythmic temporal theta bursts	Muscle
Polyspikes±slow waves	Wicket spikes	Swallowing
(Pseudo) Periodic complexes	Occipital 6 Hz spike and wave	Tongue movement
Paroxysmal lateralised epileptiform discharges	Vertex sharp waves	Electrode
	Positive sharp transients of sleep	Pulse
	K-complexes	Electrical mains

## Appendix B3. Differential diagnosis of epilepsy in children

Group	Age	Diagnosis
Infants	2 months-2 years	Stiff baby/hyperekplexia Cyanotic and pallid breath-holding spells, reflex anoxic seizure, reflex asystolic syncope Shuddering attacks Paroxysmal torticollis, extrapyramidal drug reactions, dystonia Sandifer syndrome Stereotypies, constipation, infantile gratification disorder Fabricated and induced illness Spasmus nutans Benign paroxysmal vertigo Benign myoclonus of early infancy Alternating hemiplegia of childhood Sleep disorders: rhythmic movement sleep onset disorder, benign neonatal sleep myoclonus
Childhood	2-12 years	Cyanotic and pallid breath-holding spells, reflex anoxic seizure, reflex asystolic syncope Syncope Migraine and migraine equivalents Recurrent abdominal pain Cyclic vomiting Benign paroxysmal vertigo Tics Paroxysmal torticollis Paroxysmal kinesigenic choreoathetosis Sandifer syndrome Dystonic drug reaction Constipation Stereotypies, daydreaming Gratification disorder Fabricated and induced illness Psychogenic seizures Sleep disorders: rhythmic movement sleep onset disorder, night terrors, sleep walking, talking in sleep, narcolepsy
Adolescent	12 years to adult	Syncope Migraine and migraine equivalents Psychogenic seizures Movement disorders Paroxysmal kinesigenic choreoathetosis Paroxysmal dystonic choreoathetosis Paroxysmal hereditary ataxias Tremor Tics Transient global amnesia Sleep disorders: nocturnal myoclonus, hypnic jerks, night terrors, sleep walking, talking in sleep, narcolepsy Additional non-epileptic events in children with learning difficulties Self stimulation Hyperventilation Sterotypies Sandifer syndrome Spasticity Conus Headache/pain Dystonic posturing Choreoathetosis



## Appendix C. Classification of seizure type and epilepsy syndrome

### Appendix C1. The ILAE classification of epileptic seizures

- (I) Partial (focal, local) seizures
  - (A) Simple partial seizures (consciousness not impaired)
    - (1) With motor signs
    - (2) With sensory symptoms
    - (3) With autonomic symptoms or signs
    - (4) With psychic symptoms
  - (B) Complex partial seizures (consciousness impaired)
    - (1) Simple partial onset, followed by impairment of consciousness
      - (a) With simple partial features (A1-A4), followed by impaired consciousness
      - (b) With automatisms
    - (2) With impairment of consciousness at onset
      - (a) With impairment of consciousness only
      - (b) With automatisms
  - (C) Partial seizures evolving to secondarily generalised seizures (tonic-clonic, tonic or clonic)
    - (1) Simple partial seizures (A) evolving to generalised seizures
    - (2) Complex partial seizures (B) evolving to generalised seizures
    - (3) Simple partial seizures evolving to complex partial seizures, evolving to generalised seizures
- (II) Generalised seizures (convulsive or nonconvulsive)
  - (A) Absence (petit mal) seizures
  - (B) Myoclonic seizures
  - (C) Tonic seizures
  - (D) Atonic seizures
  - (E) Clonic seizures
  - (F) Tonic-clonic (grand mal) seizures
- (III) Unclassified epileptic seizures (caused by incomplete data)

## Appendix C2. The ILAE classification of epilepsies and epilepsy syndromes

### (1) Generalised

Idiopathic generalised epilepsies with age-related onset (in order of age)

- Benign neonatal familial convulsions
- Benign neonatal convulsions
- Benign myoclonic epilepsy in infancy
- Childhood absence epilepsy
- Juvenile absence epilepsy
- Juvenile myoclonic epilepsy
- Epilepsy with generalised tonic-clonic seizures on awakening
- Other generalised idiopathic epilepsies not defined above
- Epilepsies with seizures precipitated by specific modes of activation

Cryptogenic or symptomatic generalised epilepsies (in order of age)

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

Symptomatic generalised epilepsies

- Non-specific aetiology
- Early myoclonic encephalopathies
- Early infantile encephalopathy with burst suppression
- Other symptomatic epilepsies not defined above
- Specific syndromes
- Epilepsies in other disease states

### (2) Localisation-related

Localisation-related epilepsies—idiopathic with age-related onset

- Benign epilepsy with centrotemporal spikes
- Childhood epilepsy with occipital paroxysms
- Primary reading epilepsy

Localisation-related epilepsies—symptomatic

- Epilepsia partialis continua
- Syndromes characterised by specific modes of precipitation
- Temporal lobe epilepsies

Central region epilepsies

- Frontal lobe epilepsies
- Parietal lobe epilepsies
- Occipital lobe epilepsies

Localisation-related epilepsies—cryptogenic

### (3) Epilepsies undetermined as to whether focal or generalised

With both generalised and focal seizures

- Neonatal seizures
- Severe myoclonic epilepsy in infancy
- Electrical status epilepticus in slow wave sleep
- Acquired epileptic aphasia

Other undetermined epilepsies (not defined above) with unequivocal generalised or focal features

### (4) Special syndromes

- Febrile convulsions
- Isolated seizures or isolated status epilepticus
- Seizures occurring only when there is an acute metabolic or toxic event caused by factors such as alcohol, drugs, eclampsia, non-ketotic hyperglycaemia

## Appendix D. Pharmacological treatment

### Appendix D1. Suggested choice of AEDs by seizure types in adolescents and adults (modified from NICE)

Seizure type	First-line drugs	Second-line drugs	Other options	Drugs to be avoided
Primary Generalised Tonic-clonic	Sodium valproate Carbamazepine Phenytoin Lamotrigine Topiramate	Clobazam Levetiracetam Oxcarbazepine	Primidone Clonazepam Phenobarbital	
Absence	Ethosuximide Sodium valproate Lamotrigine	Clobazam Clonazepam Topiramate		Carbamazepine Gabapentin Pregabalin Oxcarbazepine
Myoclonic	Sodium valproate Levetiracetam	Clobazam Clonazepam Piracetam Topiramate	Lamotrigine	Carbamazepine Gabapentin Pregabalin Oxcarbazepine
Tonic	Sodium valproate Lamotrigine	Clobazam Clonazepam Topiramate Levetiracetam	Primidone Phenobarbital Phenytoin	Carbamazepine Oxcarbazepine
Atonic	Sodium valproate Lamotrigine	Clobazam Clonazepam Levetiracetam Topiramate	Phenobarbital Primidone	Carbamazepine Oxcarbazepine Phenytoin
Focal with/without secondary generalisation	Carbamazepine Phenytoin Sodium valproate Lamotrigine Oxcarbazepine Topiramate Levetiracetam	Clobazam Gabapentin Pregabalin	Clonazepam Phenobarbital Primidone	

### Appendix D2. Suggested choice of AEDs by epilepsy syndromes

Epilepsy syndrome	First-line drugs	Second-line drugs	Other drugs	Drugs to be avoided
Childhood or juvenile absence epilepsy	Ethosuximide Sodium valproate Lamotrigine	Levetiracetam Topiramate		Carbamazepine Gabapentin Pregabalin Oxcarbazepine Phenytoin
Juvenile myoclonic epilepsy	Sodium valproate	Levetiracetam Lamotrigine Clobazam Clonazepam Topiramate		Carbamazepine Gabapentin Pregabalin Oxcarbazepine Phenytoin
Infantile spasms (IS)	ACTH/Steroids Vigabatrin** (first line for IS with tuberous sclerosis)	Clobazam Clonazepam Sodium valproate Topiramate	Nitrazepam	Carbamazepine Oxcarbazepine
Benign epilepsy with centrotemporal spikes or occipital paroxysms	Carbamazepine Lamotrigine Oxcarbazepine Sodium valproate	Levetiracetam Topiramate		
Severe myoclonic epilepsy of infancy	Clobazam Clonazepam Sodium valproate Topiramate	Levetiracetam	Phenobarbital	Carbamazepine Lamotrigine Oxcarbazepine
Lennox-Gastaut syndrome	Lamotrigine Sodium valproate Topiramate	Clobazam Clonazepam Ethosuximide Levetiracetam		Carbamazepine Oxcarbazepine
Landau-Kleffner syndrome	Lamotrigine Sodium valproate Steroids	Levetiracetam Topiramate		Carbamazepine Oxcarbazepine
Myoclonic astatic epilepsy	Clobazam Clonazepam Sodium valproate Topiramate	Lamotrigine Levetiracetam		Carbamazepine Oxcarbazepine

### Appendix D3. Position statement of HKES on generic AED substitution

- A narrow therapeutic range is well known for many AEDs, eg phenytoin, carbamazepine, valproate. Although a wider therapeutic range probably exists for new AEDs, serum drug concentration monitoring is not routinely available to measure the difference in AED absorption and guide the proper dosage.
- There are many case reports of adverse events or breakthrough seizures following generic substitution but systematic studies are lacking to determine the impact of generic substitution.
- According to the US Food and Drug Administration (FDA) requirement, bioequivalent generic AEDs have serum drug concentrations between 80 and 125% of the brand AED. Mathematical deduction implies that the variation in rate and extent of absorption among multiple generic AEDs (with different manufacturers) may result in up to 50% difference in serum drug concentrations.
- Switching of AEDs (brand to generic or generic to generic) may result in breakthrough seizures with serious physical and psychosocial consequences, including unemployment, injury and even death.

#### The HKES recommends the following regarding generic AED substitution

- The treating physician is allowed to choose between brand and generic AEDs at initiation of treatment and subsequent switching should be avoided whenever possible.
- Switching from brand to generic or between generics should be avoided if possible.
- We oppose automatic substitution of generic AEDs at pharmacy level.
- Before switching from brand to generic AEDs, or between different generic AEDs, verbal consent should be obtained from patient by the treating physician.
- When generic AEDs are prescribed, counselling should be given to patient to improve compliance and reduce anxiety. Adequate follow-up and monitoring logistics should be implemented wherever possible.
- Switching from brand to generic AEDs or between generic AEDs is not recommended in patients whose epilepsy is in remission.

### Appendix D4. Side-effects of AEDs

AED	Side-effects
Carbamazepine	Allergic skin reactions may be severe. Blurred vision, diplopia, ataxia and nausea common
Clobazam	Drowsiness but tolerance may develop after prolonged use
Clonazepam	Somnolence and fatigue are usually transitory
Ethosuximide	Headache, nausea, and drowsiness are usually mild and transient
Gabapentin	Somnolence, dizziness, and fatigue; emotional lability in children
Lamotrigine	Skin rash or fever usually within 8 weeks of starting treatment. Adverse effects include drowsiness, diplopia, dizziness, headache, insomnia, confusion, and hallucinations
Levetiracetam	Common undesirable effects include dizziness and somnolence. Irritability, insomnia, ataxia, tremor, headache, nausea, and affective symptoms are rare
Oxcarbazepine	Diplopia, headache, nausea, skin rash, ataxia, and confusion
Phenobarbital	Drowsiness, lethargy, mental depression, and allergic skin reactions
Phenytoin	Hypersensitivity reactions including skin rash. Dose-related side-effects include drowsiness, ataxia, and slurred speech. Coarsening of facial features, gingival hyperplasia, and hirsutism may occur rarely. Anaemias are usually responsive to folic acid. Dyskinesias, tremor, and mental confusion are rare
Piracetam	Weight gain, somnolence, nervousness, depression, and rash
Primidone	Drowsiness and listlessness are common
Sodium valproate	Sedation, tremor, weight gain, and transient hair loss has often been reported. Severe liver damage, encephalopathy, pancreatitis, transient hyperammonaemia and blood dyscrasias are rare. Amenorrhoea, irregular periods and foetal neural tube defect may occur
Topiramate	Headache, somnolence, dizziness, paraesthesia, weight loss, difficulty with memory and concentration has been reported. Increased risk of nephrolithiasis and glaucoma; rarely reduced sweating in children
Vigabatrin	Somnolence, nausea, agitation, aggression, irritability, and depression are common. Psychosis is rare. Visual field defects common and may occur after months to years of vigabatrin treatment. Visual field should be tested every 6 months

## Appendix E. Examples of factors to consider in selecting an AED in newly diagnosed epilepsy

### Example 1

F/17, College student

**Seizure types:**

**Generalised tonic-clonic seizure and early morning myoclonus**

**Syndromic diagnosis:**

**Juvenile myoclonic epilepsy**

- Valproate is the standard AED to be used but in view of its teratogenicity, other broad-spectrum AEDs may be selected.
- Topiramate has more cognitive side-effect but it may be preferred if there is co-existing migraine or morbid obesity.
- Lamotrigine is a reasonable alternative but it may worsen myoclonus; its serious allergic reaction should be made known to the patient.
- Clonazepam or clobazam may cause daytime sleepiness with issues of tolerance in the long term.
- Levetiracetam is a suitable alternative as it has a good side-effect profile.

### Example 2

M/70, retired businessman

**Seizure type:**

**Secondary generalised tonic-clonic seizure**

**Aetiological diagnosis:**

**Post-stroke epilepsy, atrial fibrillation on warfarin**

- Carbamazepine and oxcarbazepine are more likely to give rise to hyponatremia with its consequent side-effects; testing for HLA B1502 should be done before commencement of carbamazepine; oxcarbazepine is better than carbamazepine as it does not interact with warfarin.
- Phenytoin is favoured by some physicians as response to treatment is usually satisfactory, but dosage adjustment should be cautious in view of its non-linear pharmacokinetics. It may increase or decrease efficacy of warfarin.
- For sodium valproate, some side-effects (eg hand tremor) may be more common in the elderly and valproate may enhance effect of warfarin.
- Lamotrigine and levetiracetam are better tolerated in the elderly without problem of drug interaction but their use is limited by their cost. Gabapentin and pregabalin are useful if there is co-existing neuropathic pain (eg thalamic stroke) and polypharmacy (virtual absence of drug interactions).
- Topiramate may have a negative impact on cognition which may already be compromised after stroke; side-effects, eg paresthesia, may generate worries about recurrent stroke.
- Clonazepam and clobazam are sometimes useful if there is co-existing tremor, myoclonus, anxiety, sleep-related behavioural disorder, insomnia, or restless leg syndrome.
- Phenobarbitone may adversely affect cognition but advantages include low cost and availability of parenteral formulation. It is an enzyme inducer, which may reduce efficacy of warfarin.

### Example 3

F/9, schoolgirl

**Seizure type:**

**Partial motor seizure of left face with secondary generalised tonic-clonic seizure**

**Epilepsy syndrome:**

**Benign epilepsy with centraltemporal spikes (BECT)**

**Co-morbidity**

**Migraine**

- Carbamazepine and oxcarbazepine are the standard drugs of treatment but HLA B1502 status should be checked before commencement of carbamazepine.
- Sodium valproate is useful for preventing co-existing migraine; side-effects including weight gain, transient hair loss and menstrual disturbances are undesirable.
- Lamotrigine may induce serious drug rash particularly in children and very slow escalation of dose is necessary; it has not been licensed for monotherapy in children younger than 12 years old.
- Topiramate is non-enzyme inducing and also effective against migraine but it may cause anhydrosis in children.
- Levetiracetam may rarely induce behavioural disturbance especially for those with a history of psychiatric disorder; it has not been licensed for monotherapy in children younger than 16 years old.
- Gabapentin is less efficacious compared with other standard AEDs.
- Pregabalin is only licensed for treatment of adult epilepsy.
- Phenytoin is not favoured in view of its cosmetic side-effects, erratic absorption and non-linear pharmacokinetics.
- Phenobarbitone is not preferred as it may cause irritability, behavioural disturbance and cognitive impairment in children.
- Clobazam and clonazepam may cause excess daytime drowsiness; they are mainly used as adjunctive therapy instead of monotherapy.