Management of Epilepsy and Nodding Syndrome patients

A brief guide

Management during a seizure (see fig. 1)

1) Do not panic

1. Move patient away from fire, traffic, or water
2. Take away any objects that could harm the patient
3. Loosen tight clothes, remove glasses
4. Put something soft under the head
5. Turn patient on his or her side, so that saliva and mucus can run out of the mouth
6. Remain with the patient until he or she regains consciousness
7. Monitor and record the duration of the seizure
8. Let the patient rest and then resume whatever activity he was doing if he feels like it.

Some Don'ts

1. Do NOT try to put anything into the mouth

2. Do NOT give anything to drink or eat

3. Do NOT try to stop the jerking or restrain the movements.

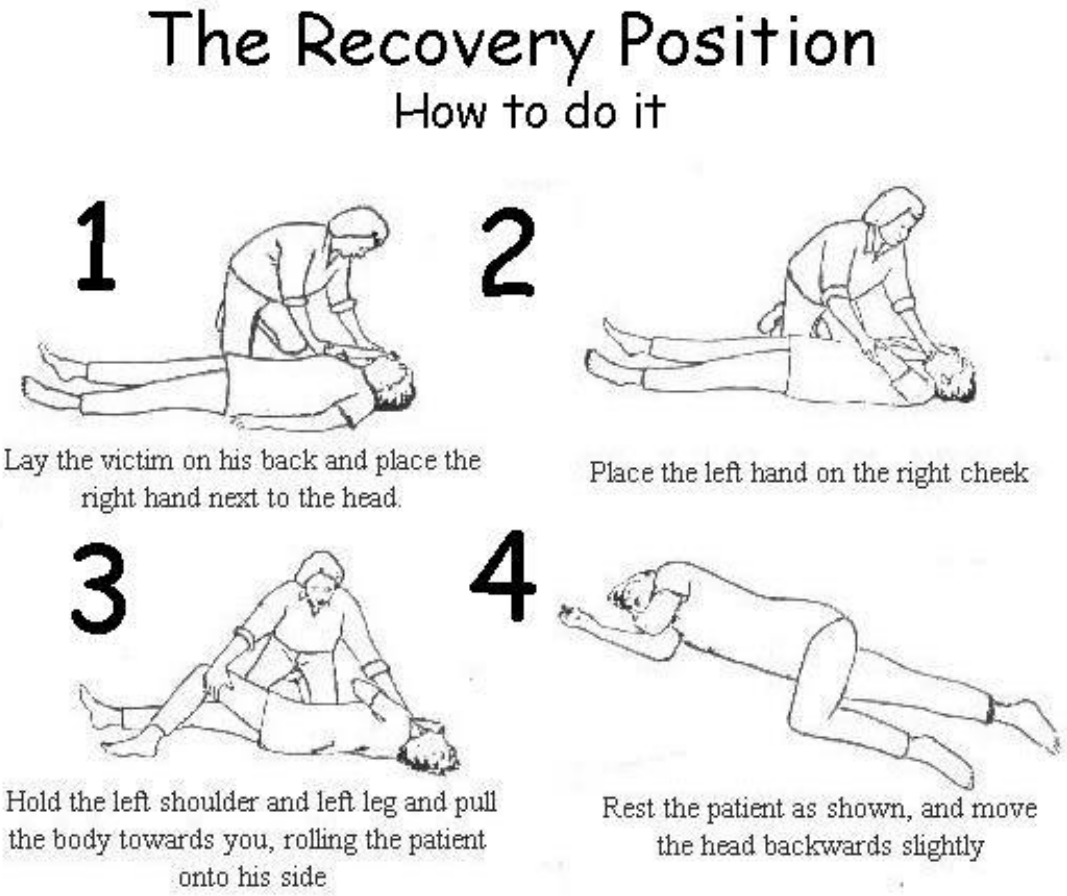

Figure 1. The coma position. Unconscious patients should be placed in this semi-prone position to minimize the risk of obstruction or inhalation of vomit.

Guiding principles to start anticonvulsant drug treatment in previously untreated patients

1. Carefully establish diagnosis.
2. Start drug treatment with one drug.
3. Start drug treatment with a small dose.
4. Gradually increase dosage until complete seizure control is achieved. This is the minimum maintenance dose.
5. The aim of the treatment is to achieve the lowest maintenance dose which provides complete seizure control.

6. A gradual introduction of an anticonvulsant (also called antiseizure drugs) can produce therapeutic effects just as fast as rapid initiation with large doses, but with fewer side-effects.

7. Severe side-effects appearing at the beginning of the treatment can indicate too rapid or too large dose increases. Side-effects to anticipate include fatigue, excess sleep need, dizziness, skin rashes or difficulty walking (ataxia).

8. If the initial drug of choice is not well tolerated, e.g., if side-effects occur or if the maximum tolerated dose does not produce seizure control, substitute the initial drug with another first line anticonvulsant.

9. A second anticonvulsant should be added gradually and the first then slowly withdrawn.

10. In case of acute withdrawal symptoms, e.g., recurrence of seizures, use diazepam as a control drug. Diazepam can be administered orally (e.g. for non-convulsive seizures in series) or through rectal administration (e.g. febrile seizures in children; convulsive status epilepticus)**

'Rectal diazepam kits' can be prepared and pre-positioned at epilepsy clinics.

The kit contains:

- **a)** a 25ml bottle of diazepam mixed with a stabilising solution, containing 1mg of diazepam in each 1ml
- **b)** a reusable 10ml syringe
- **c)** a reusable soft plastic tube to attach to the syringe for drawing up and injecting the diazepam
- **d)** a sachet of lubricant jelly

11. Regular compliance is the key to successful seizure control, and counselling the patient is the most critical factor in compliance.

Source: *Epilepsy: A Manual for Medical and Clinical Officers in Africa;* WHO, 2002 (with some changes)

RECOMMENDED TREATMENTS

Type of convulsions / seizures	First Line AED	Second Line AED	Third Line AED
Generalized convulsions (especially idiopathic generalized seizures)	Phenobarbitone	Carbamazepine	Valproate (costly)
Generalized tonic-clonic seizures, seizures during sleep and Status Epilepticus	Phenytoin *(always with empty stomach) (increments of doses only by small amounts)* Carbamazepine	Phenobarbitone	Valproate (costly)
Focal seizures	Carbamazepine	Phenytoin	Valproate (costly)
Nodding seizures	Phenobarbitone	Valproate (to be possibly avoided due to high cost) *The most common practice is to start at 10 mg/kg/day in two divided doses, then slowly titrated dose to a maximum of 30 mg/kg/day*	Phenytoin

Drug	INDICATION	DOSAGE	POSSIBLE SIDE EFFECTS	CONTRAINDICATIONS/CAUTIONS
Phenobarbitone	Indicated as first line AED for most seizure types (focal and generalized) and status epilepticus. Not indicated for absence seizures. Most affordable AED.	**Starting dose:** Children: 3 mg/kg daily Adults: initial 30-50 mg/day in adults **How to increase dose:** after one month, if seizure continue, dosage can be increased by 15-30 mg every 4 weeks, without exceeding the maximal dose for weight and age. **Maintenance dose:** Children: 3-8 mg/kg daily Adults: 30-180 mg daily (not exceeding 200 mg total daily dose) **Number of daily administrations:** Can be given in a single dose prior to sleep or in two divided doses.	**Common**: sedation, drowsiness, behavioural changes, depression, impairment of attention and memory, decreased libido and potency, ataxia, nystagmus. Hyperactivity common in children. Connective tissue disorders (long term use): shoulder pain, Dupuytren contracture (fingers bent in a fixed position) Metabolic bone disorders: rickets and osteomalacia (especially in patient with difficulty in moving) **Serious**: severe adverse skin reactions (including Steven-Steven Johnson syndrome, Toxic Epidermal Necrolysis, Drug Reaction with Eosinophilia and Systemic Symptoms) hepatic failure (also due to hypersensitivity), thrombocytopenia, agranulocytosis.	Contraindicated in patients with porphyria. Lower doses should be used in patients with liver or renal disease. Should be avoided, if possible, in pregnancy and during breastfeeding due to risk of foetal malformations and neurodevelopmental effects: if necessary, use the lowest effective dose.

Carbamazepine	Indicated for focal seizures, can be used in generalized convulsive seizure but may aggravate seizures in some generalized epilepsy syndrome. Not indicated in absence and myoclonic seizures.	**Starting dose:** Children: 5 mg/kg daily in two equally divided doses (2,5 mg/kg/dose) Adults: 200 mg daily in two equally divided doses (100 mg/dose) **How to increase dose:** after 2 weeks, if seizure continue, dosage can be increased by 5 mg/kg daily in children and by 200 mg daily in adults every 2 weeks, without exceeding the maximal dose for weight and age. **Maintenance dose:** Children 10-30 mg/kg daily in two divided doses (max 30 mg/kg total daily dose) Adults: 400-1200 mg daily in two equally dived dose (max 600 mg twice daily) **Number of daily administrations:** Two equally divided dose.	**Common**: sedation, headache, dizziness, ataxia, double vision (frequently first sign of too high dosage), nausea, diarrhoea, mild leukopenia. **Serious:** severe adverse skin reaction (see above) aplastic anaemia and agranulocytosis, cardiac conduction anomalies, very low sodium levels	Use with caution in patients with cardiac, liver, kidney and blood disease. Use with caution in pregnant women and during breastfeeding (lowest effective dose).

Phenytoin	Indicated for focal seizures and generalized tonic-clonic seizures and status epilepticus. Not indicated for absence and myoclonic seizures.	**Starting dose:** Children: 3-4 mg/kg daily in one or two equally divided doses (1,5-2 mg/kg/dose) Adults: 100-200 mg daily in one or two equally divided doses **How to increase dose:** after 1 month, if seizure continue, dosage can be increased by 25 mg in children and by 50 mg daily in adults every 4 weeks, without exceeding the maximal dose for weight and age. **Maintenance dose:** Children: 3-10 mg/kg daily in one or two divided doses (max 8 mg/kg/daily and never exceeding 300 mg total daily dose) Adults: 200-400 mg daily in one or two equally divided dose (max 400 mg total daily dose) **Number of daily administrations:** One or two equally divided dose.	**Common:** sedation, confusion, dizziness, tremor, motor twitching, ataxia, double vision, nystagmus, slurred speech, nausea, vomiting, constipation (typically dose-related). Chronic use associated with gum hyperplasia (can be prevented by careful oral hygiene and folate supplementation), acne, hirsutism. **Serious:** severe adverse skin reaction, hepatitis, polyneuropathy and cerebellar atrophy, lymphadenopathy	Lower doses for patients with kidney or liver disease. Should if possible be avoided during pregnancy and breast feeding: if necessary, use lowest effective dose)

Valproate	Indicated for all generalized seizures, including absences, myoclonic seizures and drop attacks. Can also be used in focal seizures. First line AED for Nodding Syndrome, **but very expensive and unaffordable: to be avoided when adequate alternative treatments are available (i.e. Phenobarbital)**	**Starting dose:** Children: 10mg/kg daily in two equally divided doses Adults: 400 mg daily in two equally divided doses **How to increase dose**: after 2 weeks, if seizure continue, dosage can be increased by 10 mg/kg/die in children and by 400 mg daily in adults every 2 weeks, without exceeding the maximal dose for weight and age. **Maintenance dose:** Children 20-30 mg/kg (children under 20 Kg) in 2 divided doses; Adults: 400-1800 mg daily in two equally divided dose (max 1800 mg total daily dose). **Number of daily administrations:** Two equally divided dose.	**Common**: sedation, headache, tremor, ataxia, nausea, vomiting, diarrhoea, weight gain, transient hair loss. **Serious:** encephalopathy with hyperammonaemia (drowsiness/confusion), liver failure, haemorrhagic pancreatitis, thrombocytopenia, leukopenia.	Avoid in pregnancy and during breastfeeding due to risk of foetal malformations and neurodevelopmental effects. Use with caution in patients with underlying or suspected liver disease.

***Pregnancy*:** Though no anti-epileptic drug is absolutely safe during pregnancy and lactation, the least dangerous for the foetus/infant are Phenobarbital and Carbamazepine.

During the last months of pregnancy an increase in medication is often necessary. This can be reduced again after the baby is born.

Breast milk: Most of the anticonvulsants are present in breast milk. Very occasionally phenobarbitone causes drowsiness in the baby; with phenytoin the effects are not noticeable. There is no contraindication for breast feeding.

Lack of improvement in seizure reduction

When there is no improvement at all after starting the treatment, the following reasons must be considered:

- **i.** The diagnosis is incorrect; thus, it is not epilepsy (the seizures might be fainting attacks or pseudo-seizures).
- **ii.** The medicine is incorrect; wrong drug of choice (e.g., phenytoin for generalized absences), wrong dosage (too low or too high), or wrong frequency of administration (e.g., daily dose of carbamazepine given only once a day, instead of divided over two or three times).
- **iii.** The relation between dosage and serum level is not as it should be as patient does not comply (this can also lead to status epilepticus).
- **iv.** The seizures are drug resistant (resistance to the available drugs)

Guidelines to promote compliance are given below.

Promoting compliance

The patient's adherence to any prescribed treatment will increase if the following points are considered. In the case of treatment with AEDs (before starting the treatment and during all its duration) the patient has to be warned, in a clear and understandable way, to bear in mind the points "e" to "h" listed below. Make sure that:

- **a.** The patient perceives his/her clinical condition (in this case, seizures) as a problem.
- **b.** Once the patient is convinced: that the proposed treatment has a reasonable probability of improving his/her clinical condition (i.e., decreasing the magnitude of the problem); disappearance of seizures does not mean treatment is no longer necessary.
- **c.** The side-effects (and all other inconveniences involved) are bearable and justified in terms of the perceived benefits.
- **d.** The treatment procedures are easy to follow.

e. The goal of the treatment is **the reduction of seizures to a minimum possible**. Most important is the control of seizures with impaired awareness. For some patients this could mean no more seizures, but for others only fewer seizures.

f. The treatment has no immediate effect; it takes a few weeks (two to six) before the drug reaches a protective blood level. Many patients may need a further increase of dosage.

g. The prescribed dose should not be altered by the patient and his/her family, regardless of the degree of seizure control. Only the health worker can modify the prescribed dose.

h. Abrupt interruption of drug intake should be avoided at all costs as this may precipitate continuous seizures. Provisions should be made for timely procurement of the drug. The language, the terms and the contextual meaning must be those of the patient. It is also important to enquire about the reasons for noncompliance and to deal appropriately with those reasons.

The following procedures have proven to help in promoting compliance with treatment:

1. Use of family reminders.
2. Linking drug intake to specific daily activities.
3. Increased home visits (by community health workers) with repeated explanation of:
    a. the necessity for continuous long-term treatment,
    b. possible side-effects.

A sudden discontinuation may lead to a dangerous Status epilepticus!

Source: *Initiative of support to people with epilepsy*. Division of Mental Health, World Health Organization, Geneva, 1990.

Table 1 Adaptation of the epilepsy screening questions to the local context

Questions in scientific language [37]	Questions explained and adapted to the context	Remark
1. Loss of consciousness and/or micturition and/or drooling? *Sensitivity: 87.8%* *Specificity: 90.3%*	Does the person suddenly fall for a short period of time (few seconds to minutes)? During such falls, is there saliva (foam) on the mouth and/or urine on the victim?	- Sudden fall implies that the victim has no time to hold onto a support before falling. - Micturition and drooling are usually absent during syncope, dizziness or hysteria but typically present during generalized tonic-clonic seizures.
2. Absences or sudden lapse of consciousness for a short duration? *Sensitivity: 50.0%* *Specificity: 86.6%*	Does the person suddenly stop talking/ eating/working for a short period of time (few seconds), and does not respond when you call him/her? After that, does she/he resume to what she/he was doing?	- Questions must relate to common activities such as farming, talking and eating because it is the easiest way to notice abnormal events. - If the PWE cannot recall the episodes of brief lapse of consciousness meanwhile it is reported by the caretakers, it is most likely an absence.
3. Jerky or uncontrolled movements of one or more limbs (convulsions), of sudden onset and lasting for a few minutes? *Sensitivity: 69.5%* *Specificity: 79.9%*	Does the person get sudden shaking of the whole body or just part of the body (hands, legs) and this then calms down after a short while?	Generalized tonic-clonic seizures are easily recognized and may have a local appellation. It could be helpful to ask the interviewee to mimic the abnormal movements. Ask also whether the person experiences isolated movements of the head (nodding seizures). Importantly, do not suggest answers.
4. Sudden onset of brief body sensations, hallucinations or illusions be they visual, auditory or olfactory? *Sensitivity: 37.8%* *Specificity: 80.5%*	While fully awake, does the person often complain of abnormal body sensations, or seeing/ hearing/ smelling things that are not really there for a short period (few seconds to minutes)?	Non-motor seizures are difficult to explain. The best approach is to create a scenario of visual or auditory hallucinations (seeing people who are not present, hearing voices). In some cases, the symptom is well known but had never been attributed to epilepsy. Use the local word for hallucinations when screening, if it exists.
5. Had it been said before that the subject had epilepsy or had presented epileptic seizures? *Sensitivity: 70.7%* *Specificity: 94.8%*	Ask the question using the local word for persons with epilepsy in that community.	Most families will readily answer this question. However, more tact is needed to pull out cases that are generally hidden by the family because of associated stigma [64].

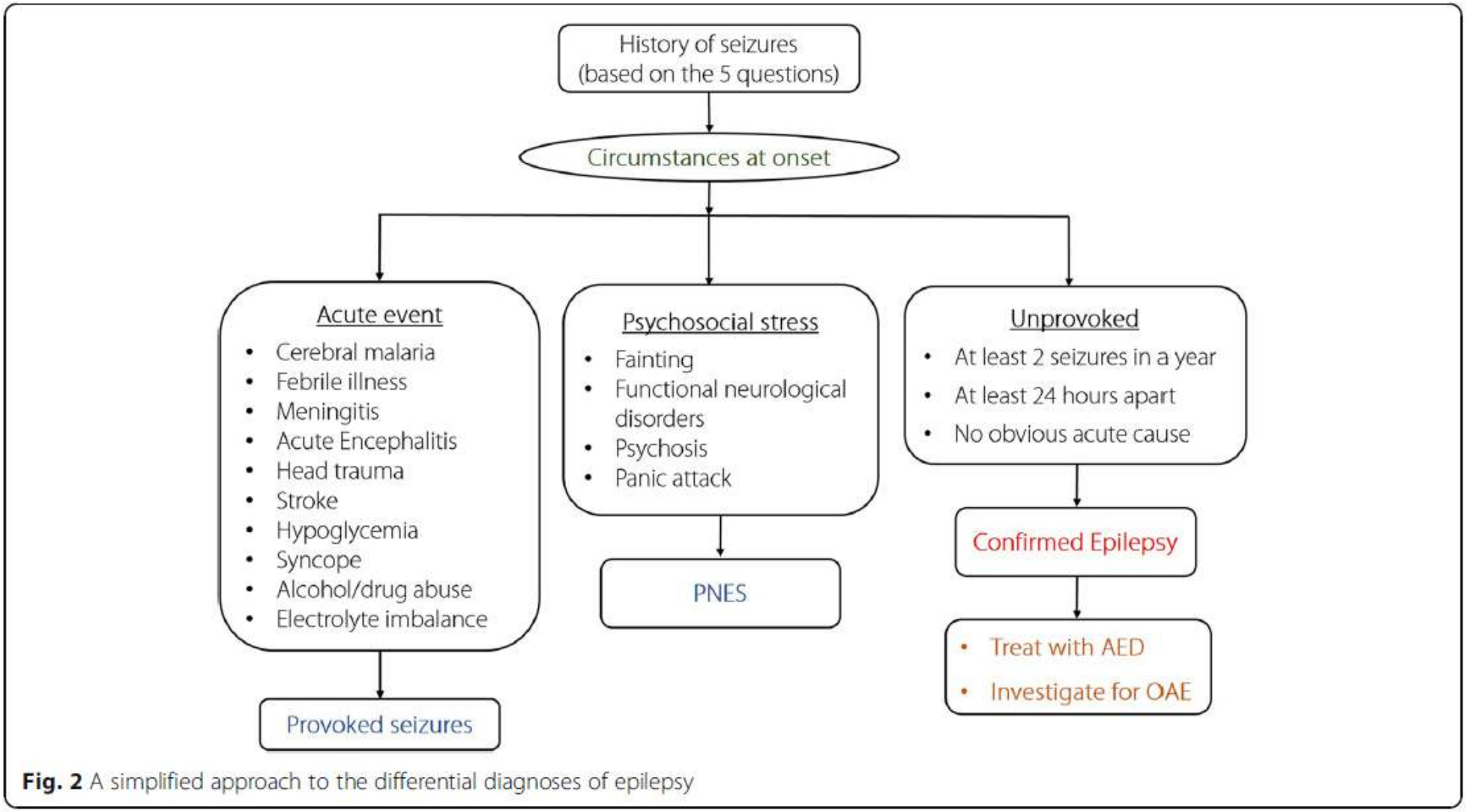

Fig. 2 A simplified approach to the differential diagnoses of epilepsy