MODULES ON EPILEPSY

MODULE IV

Management of Epilepsy

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DRUG TREATMENT FOR EPILEPSY

Importance of Initial Treatment

The first five years of treating patients with new-onset epilepsy are crucial. Here are the key treatment principles:

1. Early and Accurate Diagnosis: Ensuring an accurate diagnosis early in treatment is essential.

2. Individualized Treatment Plans: Treatment plans should be tailored to the individual patient.

3. Monitoring and Adjustment: Regular monitoring and adjustment of treatment based on patient response.

Effectiveness of Antiepileptic Drugs (AEDs)

Antiepileptic drugs (AEDs) are effective in controlling seizures for most patients. Key statistics include:

- 65% of patients with new-onset epilepsy respond well to initial AED treatment.

- 5% of patients experience seizure recurrence.

- 35% of patients have uncontrolled epilepsy despite treatment.

When initiating AED therapy:

- 50% of patients achieve seizure control with the first AED tried.

- Failures: Reasons for AED treatment failure include:

- Poor efficacy (20%).

- Intolerable side effects or idiosyncratic reactions (20%).

- Other reasons for discontinuation (10%).

Modern AEDs

Modern AEDs are diverse, effective, and safe, offering significant benefits for patients with various seizure disorders. However, the mechanisms behind seizure generation and epileptogenesis remain incompletely understood. Thus, the choice of AED should be based on clinical factors, including:

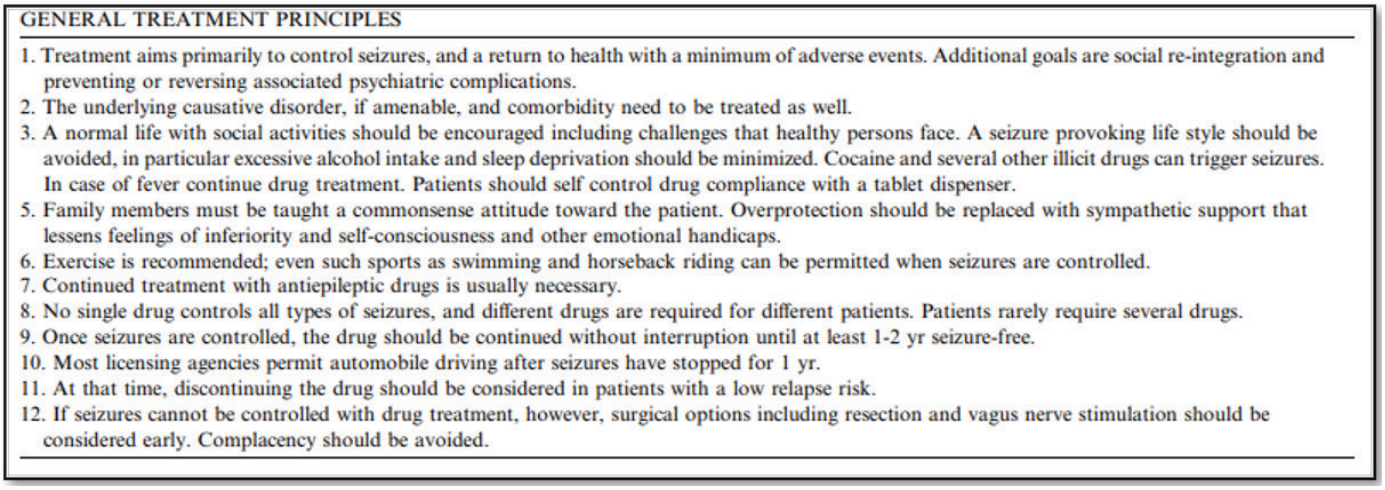
- Efficacy for the specific type of seizure or epilepsy syndrome.

- Tolerability and safety profile.

- Ease of use and pharmacokinetics.

- Need for concomitant medications due to comorbidities.

- Cost considerations.



GENERAL TREATMENT PRINCIPLES

1. Treatment aims primarily to control seizures, and a return to health with a minimum of adverse events. Additional goals are social re-integration and preventing or reversing associated psychiatric complications.
2. The underlying causative disorder, if amenable, and comorbidity need to be treated as well.
3. A normal life with social activities should be encouraged including challenges that healthy persons face. A seizure provoking life style should be avoided, in particular excessive alcohol intake and sleep deprivation should be minimized. Cocaine and several other illicit drugs can trigger seizures. In case of fever continue drug treatment. Patients should self control drug compliance with a tablet dispenser.
5. Family members must be taught a commonsense attitude toward the patient. Overprotection should be replaced with sympathetic support that lessens feelings of inferiority and self-consciousness and other emotional handicaps.
6. Exercise is recommended; even such sports as swimming and horseback riding can be permitted when seizures are controlled.
7. Continued treatment with antiepileptic drugs is usually necessary.
8. No single drug controls all types of seizures, and different drugs are required for different patients. Patients rarely require several drugs.
9. Once seizures are controlled, the drug should be continued without interruption until at least 1-2 yr seizure-free.
10. Most licensing agencies permit automobile driving after seizures have stopped for 1 yr.
11. At that time, discontinuing the drug should be considered in patients with a low relapse risk.
12. If seizures cannot be controlled with drug treatment, however, surgical options including resection and vagus nerve stimulation should be considered early. Complacency should be avoided.

Approved AEDs

The following AEDs are approved by regulatory agencies in the United States and Europe:

Common AEDs:

Acetazolamide, carbamazepine, clonazepam, clorazepate, ethosuximide, ethotoin, felbamate, gabapentin, lamotrigine, levetiracetam, mephenytoin, methsuximide, oxcarbazepine, phenobarbital, phenytoin, pregabalin, primidone, tiagabine, topiramate, trimethadione, valproate, vigabatrin, zonisamide.

- Acute Therapy for Status Epilepticus: Diazepam, fosphenytoin, lorazepam, midazolam, propofol.

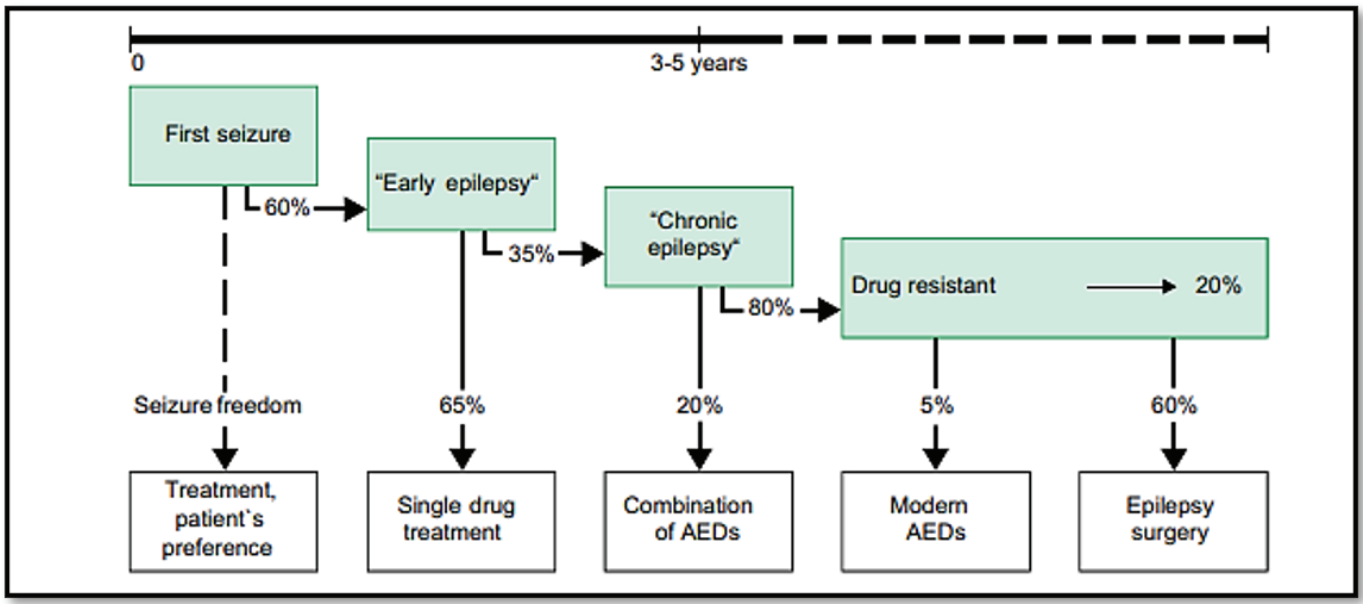


Fig. 1. Overview on management principles and estimates of seizure freedom after treatment in the first 3–5 years of new-onset epilepsy. Approximately 50% of patients become seizure free for 12 months with the first AED, if not, a change of medical regimen is achieving seizure freedom in another 20–30%. After failure of several AEDs, surgical options should be considered in suitable cases.

Recommendations

Lifestyle Changes: Adolescents should be encouraged to adopt lifestyle changes to prevent seizure precipitation.

Reevaluatison: If two or three drug regimens fail to achieve seizure control, reevaluate the epilepsy diagnosis and consider surgical options for refractory epilepsy.

AEDs provide satisfactory seizure control for most patients with new-onset epilepsy, but individualized treatment and regular reevaluation are essential for optimal outcomes.

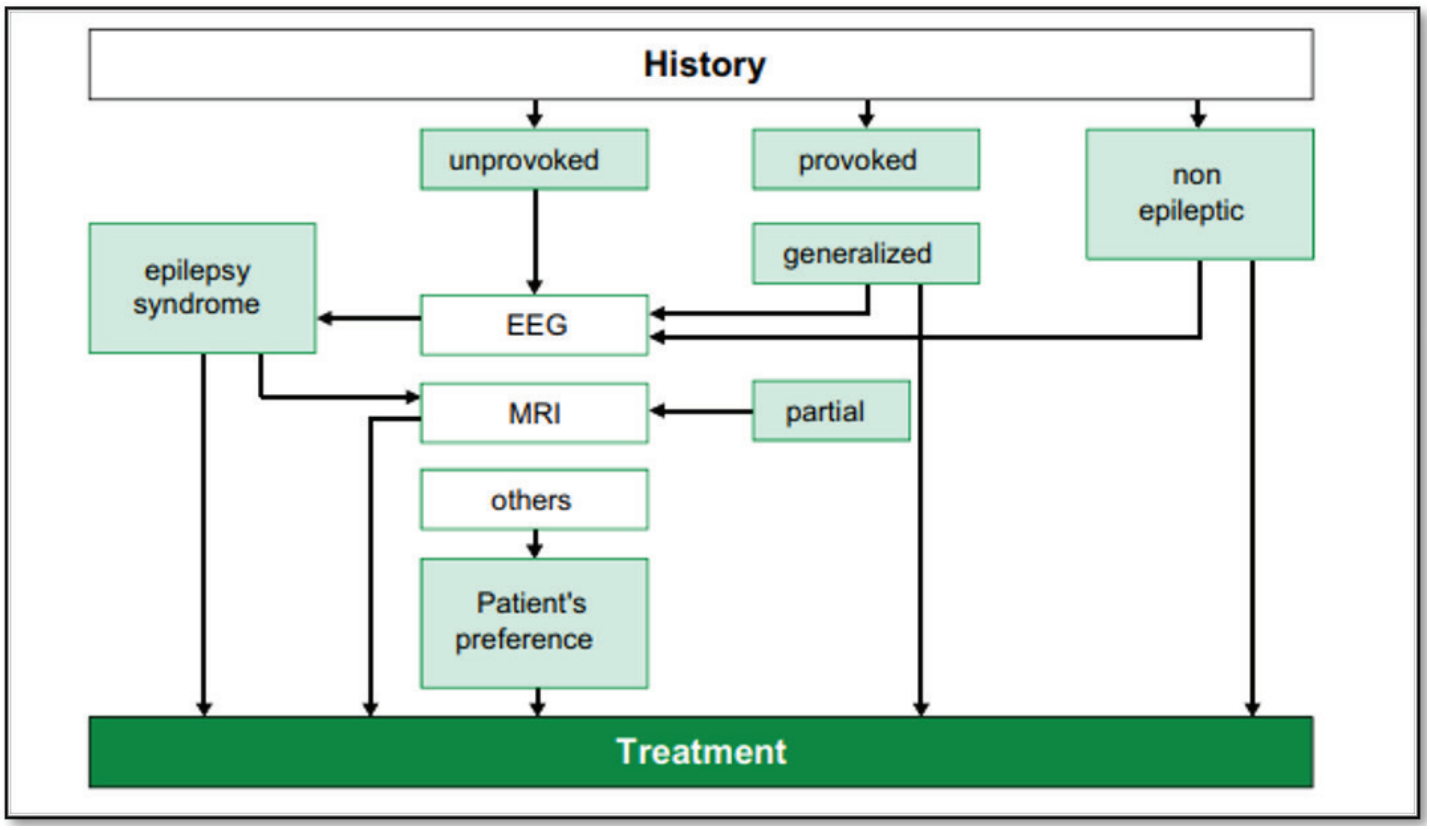


Fig. 2. Algorithm for starting drug treatment in a patient presenting with a first seizure. After a careful history, the clinical diagnosis of epilepsy is usually possible, if not, it may be prudent to observe another seizure before making a final diagnosis. In a patient with a first generalized tonic-clonic seizure, the decision to start an AED is usually based on the patient's preference after informed consent. If the diagnosis of an epilepsy syndrome can be made, as is often possible after review of the seizure and with the support of the EEG and the MRI, AED treatment is usually started, after informed consent.

STARTING TREATMENT

Assessing the Need for Drug Treatment

Starting drug treatment in patients with confirmed epilepsy involves a careful individual risk-benefit assessment. AEDs can prevent further seizures and reduce their severity, making treatment advisable for individuals with a high risk of seizure recurrence. High-risk features include:

- Symptomatic epilepsy with generalized tonic-clonic (GTC) seizures

- Complex or simple partial seizures

- Idiopathic generalized epilepsies

However, early treatment following a first GTC seizure has not been shown to improve long-term prognosis, lower mortality, or reduce the risk of injury. Some patients with a good prognosis, such as those with uncomplicated febrile seizures or benign idiopathic partial epilepsies, may not require drug treatment.

Antiepileptic drugs and their molecular targets[a]

Drug	Sodium channels	Calcium channels	GABA system	Glutamate receptors	Partial-onset seizure	Primary GTC seizure	Absence seizure	Myoclonic seizure	Infantile spasms	Lennox–Gastaut syndrome
Group A										
Phenytoin	+				+					
Carbamazepine	+				+					
Lamotrigine	+	HVA			+	+	(+)	+		
Zonisamide	+	T-type			+	+	(+)	(+)		(+)
Group B										
Phenobarbital		HVA	$GABA_A$ R	AMPA	+	+		+		
Benzodiazepines			$GABA_A$ R		+	+	+	+	(+)	(+)
Vigabatrin			GABA-T		+				+	(+)
Tiagabine			GABA transporter		+					
Ethosuximide	+?	T-type					+	(+)		
Group C										
Gabapentin		HVA α2δ	GABA turnover		+					
Pregabalin		HVA α2δ	GABA turnover		+					
Levetiracetam		HVA			+	(+)	(+)	+		

Considerations for Treatment

When deciding to start drug treatment, consider the following factors:

Adverse Events: Potential adverse events, such as central nervous system toxicity and hypersensitivity reactions, must be weighed against the benefits of treatment.

Psychosocial Consequences: The impact of another seizure, such as losing a driver's license or other social consequences, may influence the decision to start treatment.

Uncertain Diagnosis: Treatment is usually not indicated if the diagnosis of epilepsy is uncertain or if provoked seizures can be prevented without drugs.

Simplified synopsis of drug interaction properties of common AEDs

AED	Enzyme inducer (CYP)[a]	Enzyme inhibitor (CYP, UGT)	Effect of drug on disposition of other AEDs
Carbamazepine (CBZ)	Yes	No	LTG, TGB, VPA (▼▼)
Clobazam (CLB)	No	No	No relevant change
Ethosuximide (ETS)	No	No	PHT, VPA (▲), CBZ (▼)
Felbamate (FBM)	No	No	No relevant change
Gabapentin (GBP)	No	No	No relevant change
Lamotrigine (LTG)	Yes	Yes	No relevant change
Levetiracetam (LEV)	No	No	At OXC doses >900 mg (▼)
Oxcarbazepine (OXC)	Yes	No	CBZ, LTG, PHT, TGB, VPA (▼▼)
Phenobarbital (PHB)	Yes	No	CBZ, LTG, OXC, PHT, TGB, VPA (▼▼)
Phenytoin (PHT)	Yes	No	No relevant change
Pregabalin (PGN)	No	No	CBZ, LTG, PHT, TGB, VPA (▼▼)
Primidone (PRM)	Yes	No	No relevant change
Topiramate (TPM)	Yes (>200 mg/day)	No	No relevant change
Valproate (VPA)	No	Yes	PHT (▼), other AEDs (◄►)
Vigabatrin (VGB)	No	No	CBZ-E, LTG, PHB, free PHT (▲)
Zonisamide (ZNS)	No	No	No relevant change

Source. Modified from Ref. [20].

[a] CYP, cytochrome P450 system; UGT, uridine diphosphate glucuronyltransferase system; TGB, tiagabine; ◄►, no relevant change; ▼, increase in plasma concentration; ▼, decrease in plasma concentration; ▼▼, major decrease in plasma concentration.

Mechanism of Drug Action

AEDs prevent seizures by targeting various molecular mechanisms to selectively modify neuron excitability, blocking seizure-related firing while allowing normal nervous system function. Although these drugs can prevent seizures, they are not antiepileptogenic; they do not prevent epilepsy or reverse the underlying tendency to generate seizures. Antiepileptogenic strategies are under development, aiming to target plasticity mechanisms that enhance seizure susceptibility after brain insults such as trauma, status epilepticus, and neonatal hypoxia.

Recommendation: Understanding the therapeutic action of AEDs, while scientifically interesting, is of limited practical help in choosing an AED until we better understand the mechanisms of epilepsy and seizure generation for individual syndromes and patients.

Pharmacokinetics

From a clinical perspective, the ideal AED:

- Does not require plasma concentration monitoring

- Is metabolically inert

- Does not interact with other drugs

- Can be taken once or twice a day

Key points about the efficacy of AEDs:

Modern AEDs: Generally similar or better in terms of tolerability at adequate dosages for patients with partial epilepsy.

Classic AEDs: Carbamazepine provides complete seizure control in about 50% of patients, with combination or substitution regimens achieving control in an additional 10-15%. However, one in three patients remains with uncontrolled partial seizures.

Second-line AEDs such as pregabalin and zonisamide are available for combination therapy if the first drug fails to control seizures. If these drugs, individually or in combination, fail to provide seizure control, surgery should be considered. Third-line agents like clobazam, phenobarbital, phenytoin, primidone, and tiagabine are options, though they may have tolerability or safety issues and lack Class I evidence of efficacy.

Recommendation: The choice among first-line AEDs should be individualized based on the patient profile, including the type of epilepsy syndrome, tolerability, safety, pharmacokinetics, need for concomitant medications, and cost. Modern AEDs are generally preferred over classic AEDs for the treatment of partial seizures.

Treatment of Generalized Seizures

Recommended AEDs for Generalized Seizures

Typical absence seizures, juvenile myoclonic epilepsy, and related idiopathic generalized epilepsies require different treatment strategies than partial epilepsies. AEDs are often tested and licensed mainly for partial epilepsies, leading to inappropriate generalizations about their use in "epilepsy."

Key points about specific AEDs:

Contraindications: Gabapentin, carbamazepine, oxcarbazepine, and phenytoin can induce myoclonic seizures, while vigabatrin and tiagabine can induce absence seizures. These drugs are contraindicated for idiopathic generalized epilepsies.

First-Line Treatment: Valproate remains the drug of choice for idiopathic and symptomatic generalized epilepsy, despite its disadvantages like weight gain and teratogenicity. Lamotrigine and topiramate are also used but may have lower efficacy than valproate.

For absence seizures, first-line therapy includes valproate, ethosuximide, and lamotrigine, alone or in combination. Combinations of these drugs may be needed for resistant cases. Valproate controls a significant proportion of absences, GTC seizures, and myoclonic jerks but may be unsuitable for some women.

Recommendation: The choice among first-line AEDs should be based on the specific seizure type and individual patient characteristics. Modern AEDs should be preferred over classic AEDs when starting treatment for generalized seizures.

ADVANTAGES OF MODERN ANTIEPILEPTIC DRUGS

Modern AEDs generally induce fewer adverse drug interactions and result in fewer hormonal and metabolic disturbances during long-term use compared to classic AEDs. They are also associated with a lower rate of major malformations and hypersensitivity reactions.

Recommendation: Modern AEDs should be preferred over classic AEDs when starting drug treatment for new-onset epilepsy, considering individual patient characteristics and potential adverse effects.

Finding the Optimal Dose
The drug of choice for a particular type of epilepsy should be started at the lowest effective dose. Gradual titration to the average effective dose is advisable, as rapid titration can increase the risk of adverse reactions.

Recommendation: Slow titration up to average maintenance doses is generally advisable to avoid unnecessary adverse events. Higher-than-average doses should only be considered if seizure control is not achieved at average doses.

Single-Drug vs. Add-On Therapy

When single-drug therapy fails to control seizures, adding a second drug or switching to monotherapy with a different AED are common options. There are no conclusive data favoring either approach; the choice should be individualized based on the patient's response and adverse effects.

Recommendation: For patients with severe idiosyncratic reactions, substitution monotherapy is preferable. Otherwise, evaluating combination therapy first and slowly tapering the first drug if needed is a pragmatic approach. Modern AEDs, which have fewer adverse drug interactions, are better suited for combination therapy.

Advantages of Modern AEDs:

Absence of Drug Interactions: This is crucial for long-term treatment, as many patients with epilepsy require AEDs for life and often take additional medications for comorbid conditions.

Combination Therapy: Modern AEDs are better suited for combination therapy due to their minimal interaction with other drugs.

Clinically relevant effect of AEDs on the disposition of other drugs

AED	▼[a]	▲	Comments
Benzodiazepines	No relevant change	No relevant change	Higher sedation when taken with other sedating drugs (e.g., alcohol, PHB)
Carbamazepine	Anticoagulants, quinidine, contraceptives, corticosteroids, cyclosporine A, folate, digitalis glycosides, donezepil, doxycycline, felodipine, mebendazole, methadone, muscle relaxants, nifedipine, nimodipine, praxiquantel, theophylline, verapamil	Diltiazem	Lithium neurotoxicity may be functionally increased with comedication of AED. MAO inhibitors contraindicated
Felbamate	No relevant change	No relevant change	
Gabapentin	No relevant change	No relevant change	
Lamotrigine	Lower efficacy of oral contraceptives	Discontinuation of oral contraceptives may increase plasma concentration in some patients	Compromised efficacy of oral contraceptives has been reported in some patients
Levetiracetam	No relevant change	No relevant change	Partly metabolized by non-hepatic hydrolysis
Oxcarbazepine	Felodipine, contraceptives, nifedipine, nimodipine	No relevant change	Lithium neurotoxicity cannot be ruled out with comedication of OXC; MAO inhibitors contraindicated
Phenobarbital	Anticoagulants, quinidine, contraceptives, corticosteroids, cyclosporine A, diltiazem, digitalis glycosides, donezepil, doxycycline, felodipine, folate, griseofulvin, haloperidol, mebendazole, methadone, metoprolol, nifedipine, nimodipine, metronidazole, muscle relaxants, praxiquantel, propanolol, tacrolimus, tamoxifen, theophylline, verapamil	No relevant change	Methotrexate toxicity may be functionally increased with comedication of AED
Phenytoin	Anticoagulants, quinidine, contraceptives, corticosteroids, cyclosporine A, digitalis glycosides, donezepil, doxycycline, folate, mebendazole, methadone, muscle relaxants, nifedipine, nimodipine, praxiquantel, theophylline, verapamil	Diltiazem, disulfiram	Lithium neurotoxicity may be functionally increased with comedication of AED; MAO inhibitors contraindicated
Pregabalin	No relevant change	No relevant change	Pregabalin may cause peripheral edema. Exercise caution when co-administering pregabalin and thiazolidinedione antidiabetic agents
Primidone	See PHB	See PHB	
Tiagabine	No relevant change	No relevant change	
Topiramate	Contraceptives (TPM >200 mg/day),	No relevant change	
Vigabatrin	No relevant change	No relevant change	
Valproate	Itroconazole	Anticoagulants	VPA may functionally increase anticoagulation
Zonisamide	No relevant change	No relevant change	

Source. Modified from Refs. [19,20].

Abbreviations: See Table 5.

[a] ▼, Efficacy of specified drug may be lower with comedication of specified AED; ▲, toxicity of specified drug may be higher with comedication of specified AED; ◄►, no relevant change in disposition.

DRUG-RESISTANT EPILEPSY

Definition and Prevalence

Defining drug-resistant epilepsy is complex. Broadly, all epilepsy can be considered drug-resistant since AEDs only prevent seizures without addressing the underlying pathological state. In a study by Kwan and Brodie in Glasgow, of 470 patients who had never received an AED, 301 (64%) became seizure-free for at least 12 months during treatment. However, a significant number did not respond to initial treatments due to lack of efficacy, intolerable side effects, idiosyncratic reactions, or other reasons.

Seizure Freedom: Among the 248 patients who did not respond to the first drug, only 79 (32%) subsequently became seizure-free.

Treatment Failure: Only 4% responded to a third drug, and 3% responded to two drugs.

Despite these findings, newer studies suggest that 20-30% of patients with apparent drug-resistant seizures may eventually enter remission after changing drug regimens, providing hope even after years of uncontrolled epilepsy.

Causes of Drug Resistance

Several factors contribute to drug resistance in epilepsy:

Incorrect Diagnosis: Treating the wrong type of epilepsy with inappropriate drugs can exacerbate seizures.

Altered Drug Permeability: Changes in drug permeability across the blood-brain barrier, involving multidrug transporters like P-glycoprotein, can limit drug penetration into the brain.

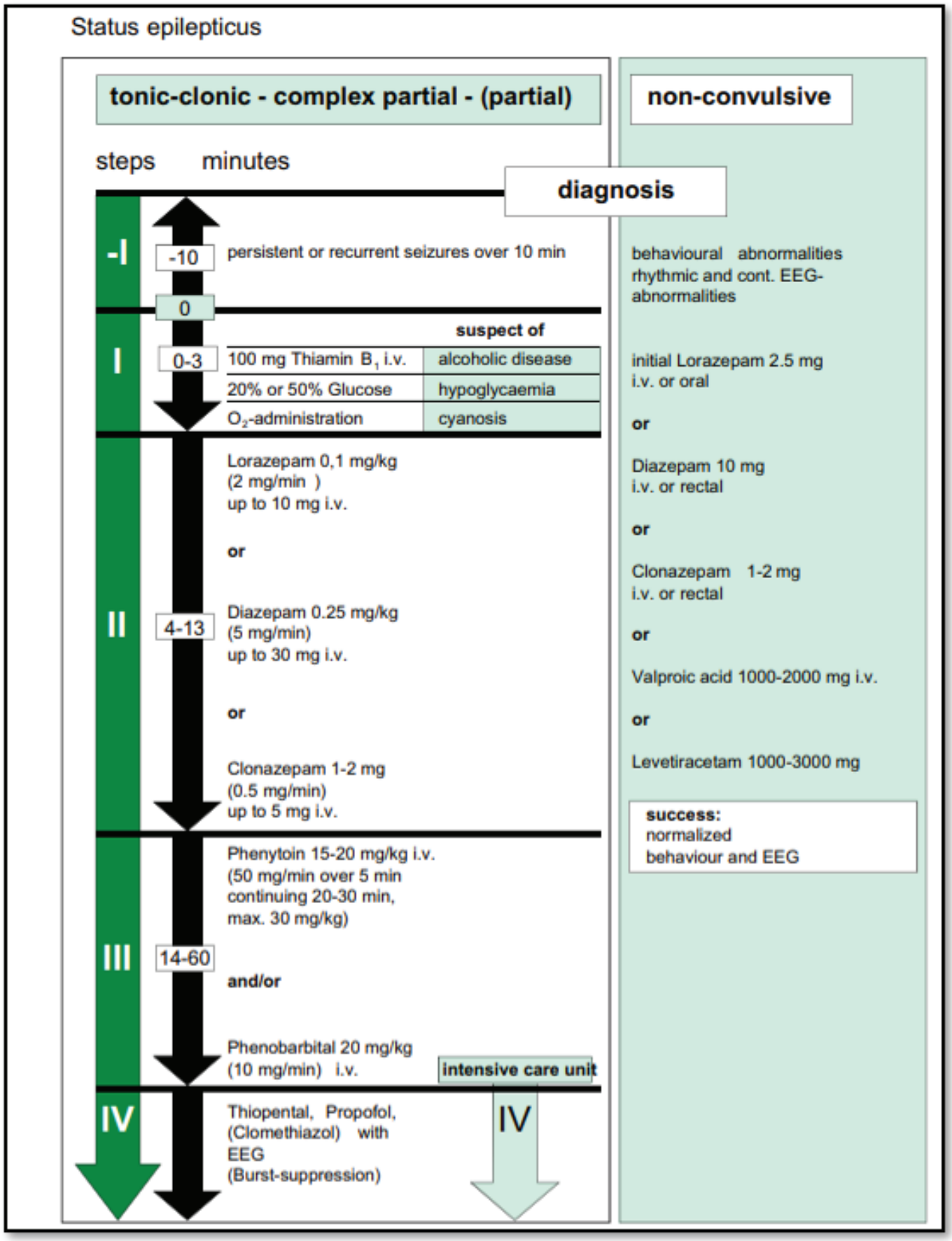


Fig.3. Treatment of status epilepticus.

Reduced Target Sensitivity: Reduced sensitivity to use-dependent blockade of voltage-dependent Na+ channels in carbamazepine-resistant patients is another mechanism.

New-generation AEDs, while useful are often unable to reverse drug-resistant epilepsy in most patients.

Consequences of Poor Seizure Control

Poorly controlled seizures have significant medical, social, and economic consequences:

Medical Risks: Increased risk of death, physical injury, cognitive impairment.

Psychosocial Problems: Reduced quality of life, higher morbidity, and mortality.

Economic Costs: Increased healthcare costs due to frequent seizures.

Limitations of Current Treatment

Prophylactic Treatment

Prophylactic treatment with anticonvulsant drugs after head injury can reduce early posttraumatic seizures but does not prevent the development of long-term epilepsy. Similarly, early treatment after a second tonic-clonic seizure does not improve long-term outcomes. The challenge is to develop novel treatment strategies that can address these drug failures and prevent seizure aggravation.

Seizure Aggravation

Seizure aggravation is a significant limitation of current AEDs, particularly in idiopathic generalized epilepsies:

Typical Absence Seizures: Can be increased by carbamazepine, vigabatrin, tiagabine, and gabapentin.

Juvenile Myoclonic Epilepsy: Often aggravated by carbamazepine and sometimes by phenytoin and other AEDs.

Generalized Myoclonic Seizures: Primidone and phenobarbital may worsen absence seizures.

Broad-spectrum AEDs like valproate, lamotrigine, and topiramate are effective at controlling various seizure types without causing excessive aggravation.

While AED treatment benefits most patients, it does not prevent epilepsy in at-risk individuals or drug-resistant epilepsy. Care should be taken to avoid drugs that exacerbate specific seizure types.

Emergency Treatment

Single Seizure

A single seizure usually lasts 1-2 minutes and does not require emergency AED treatment. Preventing injury during the seizure is crucial. This includes placing a blanket or pillow under the head, loosening clothing around the neck, and rolling the patient onto their side to prevent aspiration. Emergency antiepileptic drug treatment should be reserved for status epilepticus or multiple seizures.

Status Epilepticus

Repeated or continuous seizures lasting longer than 5-10 minutes require immediate treatment. Psychogenic nonepileptic status should be considered if standard therapy fails.

Recommendation: Avoid invasive drug treatment for single seizures or when the epilepsy diagnosis is uncertain. Immediate high-dose emergency treatment is necessary for confirmed status epilepticus.

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Undertreatment

Importance of Adequate Dosing

Undertreatment in patients with uncontrolled epilepsy due to suboptimal dosing can prevent seizure remission. In patients with uncontrolled epilepsy, a dose increment should be considered unless there are symptoms and signs of central nervous system or other organ drug toxicity. Studies show that increasing the dose led to seizure remission in as many as one in three patients presenting with uncontrolled seizures.

Recommendation: Treatment should be kept simple. Avoid unnecessary diagnostic or therapeutic interventions with an unfavorable risk-benefit balance. Ensure the diagnosis of epilepsy is certain before initiating drug treatment. Avoid combination therapy and enzyme-inducing agents if possible. Both overtreatment and undertreatment should be avoided.

NEEDS OF SPECIAL PATIENT GROUPS

Elderly Patients

The elderly often require more cautious dosing due to changes in pharmacokinetics and increased sensitivity to adverse events. High comorbidity in this population necessitates careful management to avoid disturbing drug interactions. Compliance can be challenging due to cognitive decline and multimorbidity.

Recommendations:

Prefer nonmetabolized, nonenzyme-inducing AEDs like gabapentin, lamotrigine, and levetiracetam over classic enzyme-inducing AEDs like carbamazepine.

- Use slow dose escalation and lower-than-average dosages.

- Avoid AED combination therapy when possible.

- Provide clear written instructions.

- Monitor for nonconvulsive status epilepticus.

Adolescents

Adolescents may struggle with compliance and experience significant stress from seizures, medication side effects, and social issues. Hormonal changes and weight fluctuations can occur with AED therapy.

Recommendations:

- Ensure good motivation, support from parents and healthcare providers, and a positive attitude toward treatment.

- Monitor for endocrine abnormalities such as weight changes and polycystic ovaries.

- Avoid enzyme-inducing AEDs that lower the efficacy of oral contraceptives.

- Lifelong therapy is often required for conditions like juvenile myoclonic epilepsy.

- Consider surgery for drug-resistant epilepsy, such as mesial temporal lobe epilepsy.

Women

Women with epilepsy face unique reproductive and general health concerns. They need regular review and appropriate information about the impact of their treatment on health and pregnancy.

Recommendations:

- Monitor for reproductive dysfunction symptoms like irregular menstrual cycles and weight gain.

- Use nonenzyme-inducing AEDs and consider newer AEDs like lamotrigine for those who develop reproductive issues.

- Provide pre-pregnancy counseling, including alternative contraceptive measures if enzyme-inducing AEDs are used.

- Use folate supplementation and the lowest effective AED dose during pregnancy.

- Monitor and manage AED dosage adjustments during pregnancy based on clinical symptoms.

Menopause

Menopausal women with epilepsy are at risk for osteoporotic fractures and may require treatment for osteoporosis. Hormone replacement therapy may affect seizure frequency.

Recommendation: Monitor for osteoporosis and provide appropriate treatment if necessary. Manage AED therapy to minimize adverse effects on bone health.

Men

Men with epilepsy may experience sexual dysfunction and weight gain, particularly with enzyme-inducing AEDs.

Recommendation:

Prefer weight-neutral and nonenzyme-inducing AEDs. Monitor for sexual dysfunction and avoid sedative AEDs when possible.

Persons with Mental Health Disorders

Patients with epilepsy have higher rates of depression, anxiety, and suicidal ideation. Managing these conditions is crucial for improving quality of life.

Recommendations:

- Treat depression and anxiety with appropriate medications like serotonin reuptake inhibitors and buspirone.

- Avoid classic AEDs that may contribute to mood disorders.

- Consider mood-stabilizing AEDs like lamotrigine and pregabalin.

- Use vagus nerve stimulation if both seizure control and mood stability are resistant to drug treatment.

Stopping Treatment

Discontinuing AEDs can be successful in some patients, but there is a risk of relapse. Long-term seizure control off AEDs can be achieved in about one in three patients with new-onset epilepsy.

Recommendation:

Planned discontinuation of AEDs in seizure-free patients should be approached cautiously, with an understanding of the high risk of recurrence. Consider the patient's individual circumstances and the likelihood of regaining seizure control if a relapse occurs.

NONPHARMACOLOGICAL THERAPY

Nonpharmacological therapy for epilepsy typically serves as an adjunct to drug treatment, focusing on preventing seizure triggers or utilizing surgical interventions. These methods are particularly valuable for patients with drug-resistant epilepsy.

Avoiding Seizure Precipitation

Nonpharmacological measures play a critical role in managing seizures, especially in adolescents with juvenile idiopathic generalized epilepsies. Key strategies include:

Regular Sleep Schedule: Maintaining a consistent sleep pattern is essential. Sleep onset should not vary by more than two hours.

Lifestyle Changes: Adolescents and adults with epilepsy should avoid activities that disrupt sleep and involve substance abuse or high stress, as these can trigger seizures.

Reflex Epilepsies: Specific interventions can prevent seizures in rare reflex epilepsies. For instance:

Reading Epilepsy: Patients can stop reading when experiencing perioral reflex myoclonias to avoid a generalized tonic-clonic (GTC) seizure.

Photosensitivity: Watching television from a distance, using small screens in well-lit rooms, and wearing polarized sunglasses can help prevent photic-induced seizures.

Regular sleep, stress reduction, and avoiding specific seizure triggers are crucial nonpharmacological strategies. These measures can enhance the efficacy of AEDs and sometimes eliminate the need for medication in reflex epilepsies.

Resective Surgery

Resective surgery is a standard treatment for properly selected patients with drug-resistant partial epilepsy, particularly mesial temporal lobe epilepsy. This procedure involves removing localized seizure-generating tissue.

Effectiveness: Approximately 25-30% of patients with temporal lobe epilepsy become seizure-free and no longer require AEDs, while another 25-30% become seizure-free or nearly seizure-free with continued AED treatment.

Selection Criteria: Successful surgery depends on the localization and extent of the epileptogenic zone, MRI findings, and a thorough preoperative evaluation.

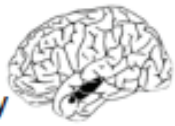
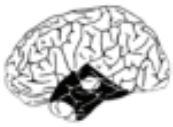
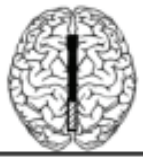
Epilepsy Surgery	
Procedure	Clinical Use
Selective Amygdala-hippocampektomy 	Ammonshornsclerosis or other pathology of the mesial temporal lobe
Tailored Temporal lobe resection 	Temporal lobe lesions or cryptogenic temporal lobe epilepsy
Topectomy (Lesionectomy) 	Extra-temporal lobe lesions
Hemispherectomy Hemispherotomy 	Hemispheric lesions or encephalitis
Topectomy transsections* 	Lesions close to eloquent brain areas
Subpial transsections* 	Lesions in eloquent brain areas
Isolated lobar resection* 	Extended lesions (developmental, post-encephalitic)
Multiple lobar Resections* 	Extended lesions (developmental, post-encephalitic)
Callosotomy* (Two-thirds or total) 	Drop attacks (Lennox-Gastaut-Syndrome)

Fig. 11. Overview of procedures for epilepsy surgery. * indicates mostly palliative interventions which rarely result in complete seizure freedom, this includes callosotomy which is thought to stop drop attacks.

Resective surgery is highly effective for suitable patients with drug-resistant temporal lobe epilepsy, offering a significant chance of seizure freedom and the possibility of discontinuing AEDs.

Neurostimulation

Neurostimulation methods, such as vagus nerve stimulation (VNS) and brain stimulation, are valuable for patients who cannot undergo resective surgery.

Vagus Nerve Stimulation: Intermittent electrical stimulation of the left vagus nerve can reduce the number of partial seizures by one-third. Patients can activate the device with a magnet when they sense a seizure.

Adverse Effects: These may include voice changes, cough, and hoarseness, which typically resolve within months.

Recommendation: Vagus nerve stimulation is a reasonable palliative option for patients who cannot have surgery or for whom surgery has been unsuccessful.

Ketogenic Diet

The ketogenic diet is a high-fat, low-carbohydrate, adequate-protein diet that has been used to treat refractory epilepsy since the 1920s. It mimics the biochemical effects of starvation, inducing ketosis.

Effectiveness: The diet is particularly effective in children with refractory epilepsy. If effective, it should be continued for 1-2 years.

- Recent Developments: The Atkins diet, a less restrictive form of the ketogenic diet, also induces ketosis and may help reduce seizures.

The ketogenic diet is an option for drug-resistant epilepsy, especially in children, when other treatments like resective surgery and VNS are not viable. Regular monitoring and a multidisciplinary approach are essential for managing potential side effects and ensuring nutritional adequacy.

Nonpharmacological therapies, including lifestyle modifications, resective surgery, neurostimulation, and dietary interventions, offer valuable adjunctive or alternative options for managing epilepsy, particularly in cases where drug treatments are insufficient. These approaches should be tailored to the individual needs and circumstances of each patient to maximize efficacy and improve quality of life.

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