



Antiseizure Drug **محاضرة:**

Nour Abu Laila **الصيدلانية:**



لجان الرفعات



Seizure :-

# Antiseizure Drugs

\* نوبة تَسْزِجَاتٍ نَاتِجَةٌ عَنِ

Abnormal discharge

بِالنَّوَاحِ neuron ، سَهْوَاتٍ زِيَادَةٍ بِالنَّوَاحِ

neuron ، هَرَسٍ ، لِيَضَاعَ إِذَا صَارَتْ

مَتَكَرِّرَةً بِتَسْمِيَةِهَا Epilepsy

\* أَمَا إِذَا أَهَمَّتْ مَرَّةً وَمَانَعَادَتْ

فَهِيَ Seizure ، وَبِتَصَرُّفٍ عِنْدَ

الْأَسْطِضَاءِ الَّتِي يَنْزِلُ عِنْدَهُمُ الْمَسْكُورِيُّ

كَثِيرٌ .

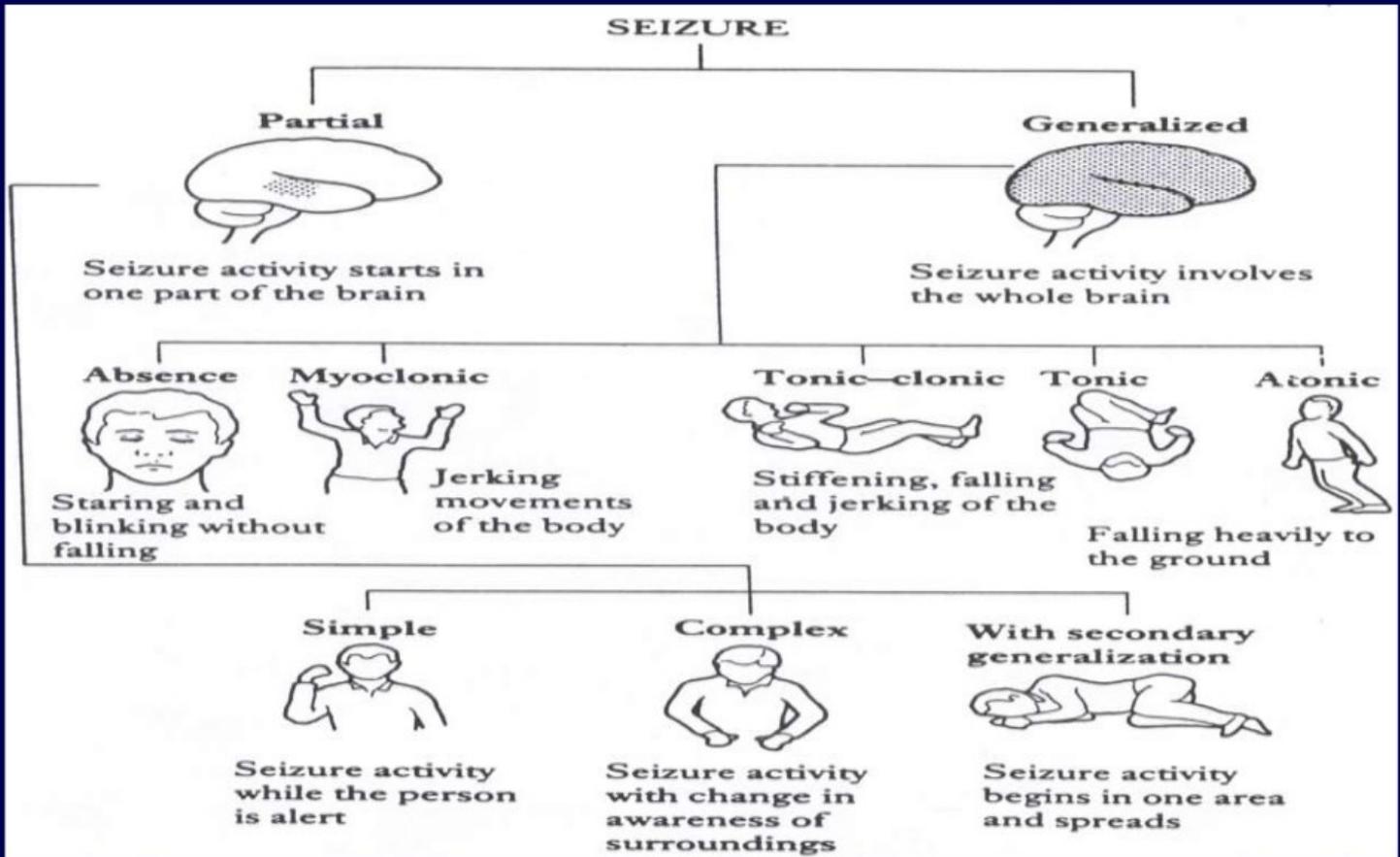
Pharmacology II

Dr. Heba Khader

اللَّهُمَّ اغْفِرْ لِحَيِّنَا وَمَيِّتِنَا وَشَاهِدِنَا وَغَائِبِنَا، وَصَغِيرِنَا  
وَكَبِيرِنَا، وَذَكَرِنَا وَأَنْثَانَا، اللَّهُمَّ مِنْ أَحْيَيْتَهُ مِنَّا فَأُحْيِهِ عَلَيَّ  
الْإِسْلَامَ وَمِنْ تَوَفَّيْتَهُ مِنَّا فَتَوَفَّهُ عَلَيَّ الْإِيمَانَ اللَّهُمَّ لَا تَحْرِمْنَا  
أَجْرَهُ، وَلَا تَضِلَّنَا بَعْدَهُ.



# Classification of Epileptic Seizures





# First Aid for Seizure

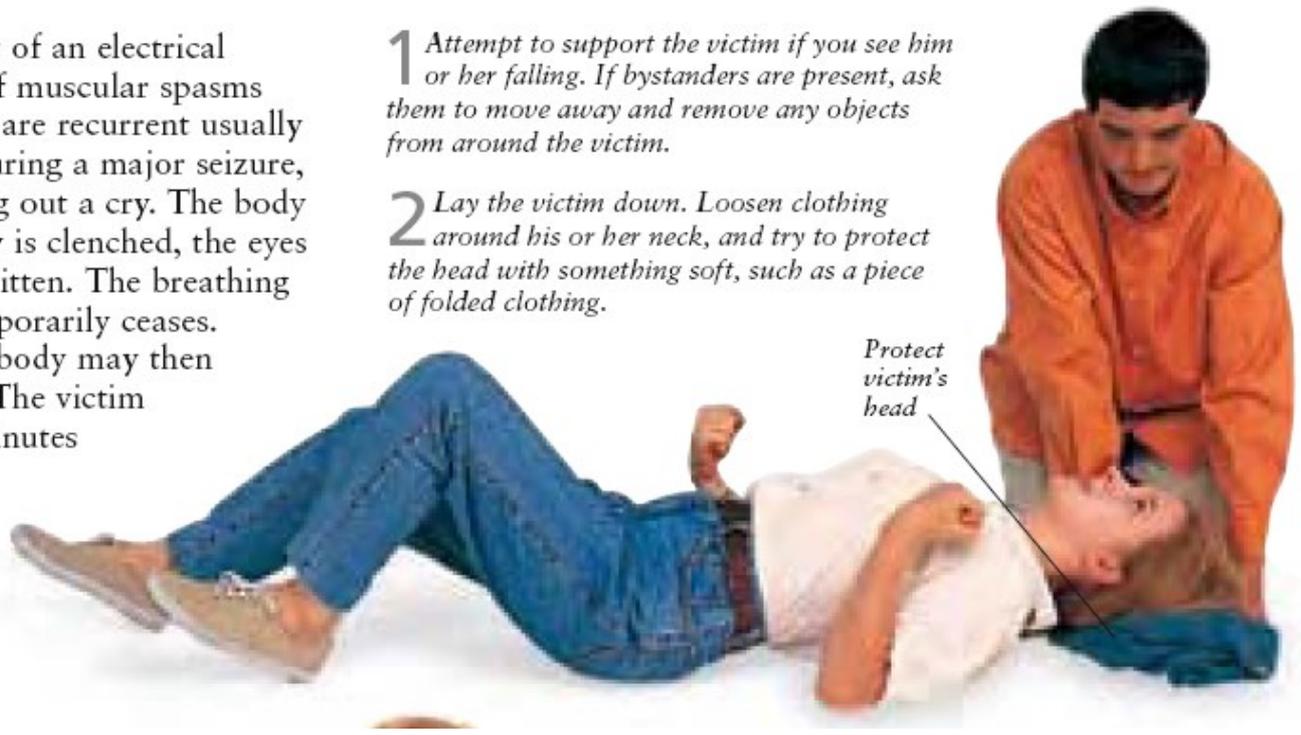
اندا سفت شخضا صهار بدو يوقع  
اون شي بتمسكو وتنزلوعنه الاكرفن  
بيظرف عشان ما يتأثر واذا في راسي  
صولين رقبتي يمنعو يتنفس بنشيلو .

٢) فتأخذ اذا يتنفس أولا ، اذا اه ضلعت نتركته  
ولا تحاول نشيتو ، ممكن تستمر صلاي احواله 3-4 min

t of an electrical  
of muscular spasms  
are recurrent usually  
uring a major seizure,  
g out a cry. The body  
v is clenched, the eyes  
bitten. The breathing  
porarily ceases.  
body may then  
The victim  
inutes

- 1 Attempt to support the victim if you see him or her falling. If bystanders are present, ask them to move away and remove any objects from around the victim.
- 2 Lay the victim down. Loosen clothing around his or her neck, and try to protect the head with something soft, such as a piece of folded clothing.

Protect victim's head



بعد ما خلصت اول اى 3 مقايعة  
بتكون خديت التشنجات بس  
لسة مش واعي ف لازم تقعدو  
بحاله تكون مريحة إلو زكي الصرة ، صاي الحالة بتساعدو عمل التنفس ، وفضل وافتح عنود

# First Aid for Seizure



**3** When the seizures have finished, place the victim in the recovery position (p.292). Check the victim's breathing and pulse at regular intervals, and be prepared to resuscitate if necessary (see ABC of resuscitation, p.290).

**4** If the victim has a severe seizure, in which he or she remains unconscious for more than 10 minutes or convulses for more than 5 minutes, or if the person has repeated seizures, call an ambulance. Stay with the victim and monitor breathing and pulse until the ambulance arrives.

✗ كل العملية مش لازم توخذ أكثر من 10 min  
اذا هنل عنش واعي لمدة أطول نطلب الإسعاف

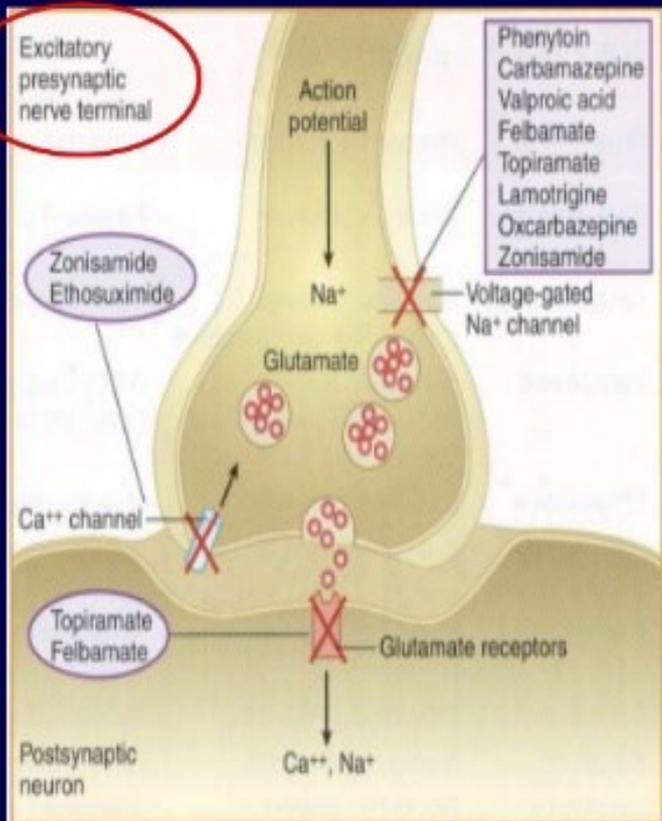
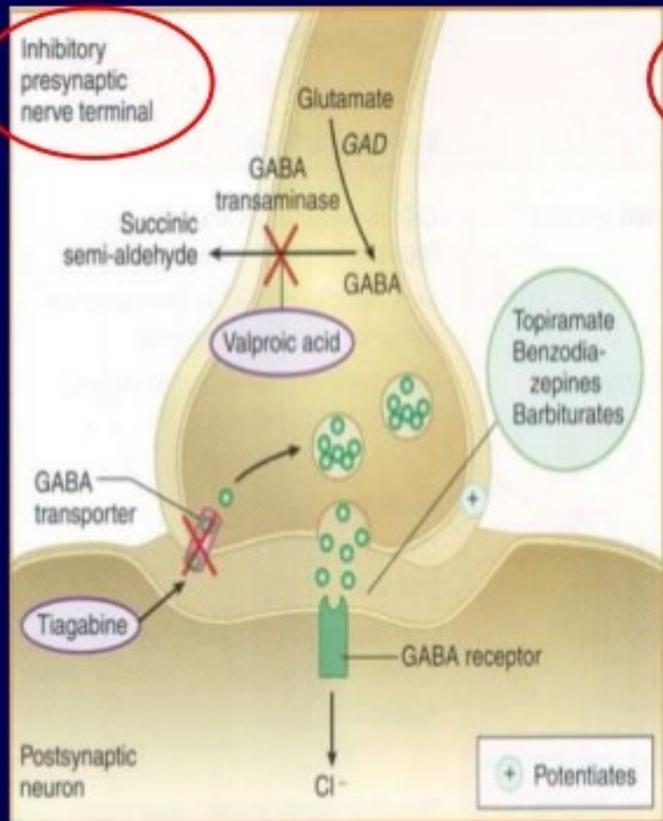
**WARNING**

- Do not use force in an attempt to restrain the victim.
- Do not put anything in the victim's mouth.





# Mechanism of action of AEDs











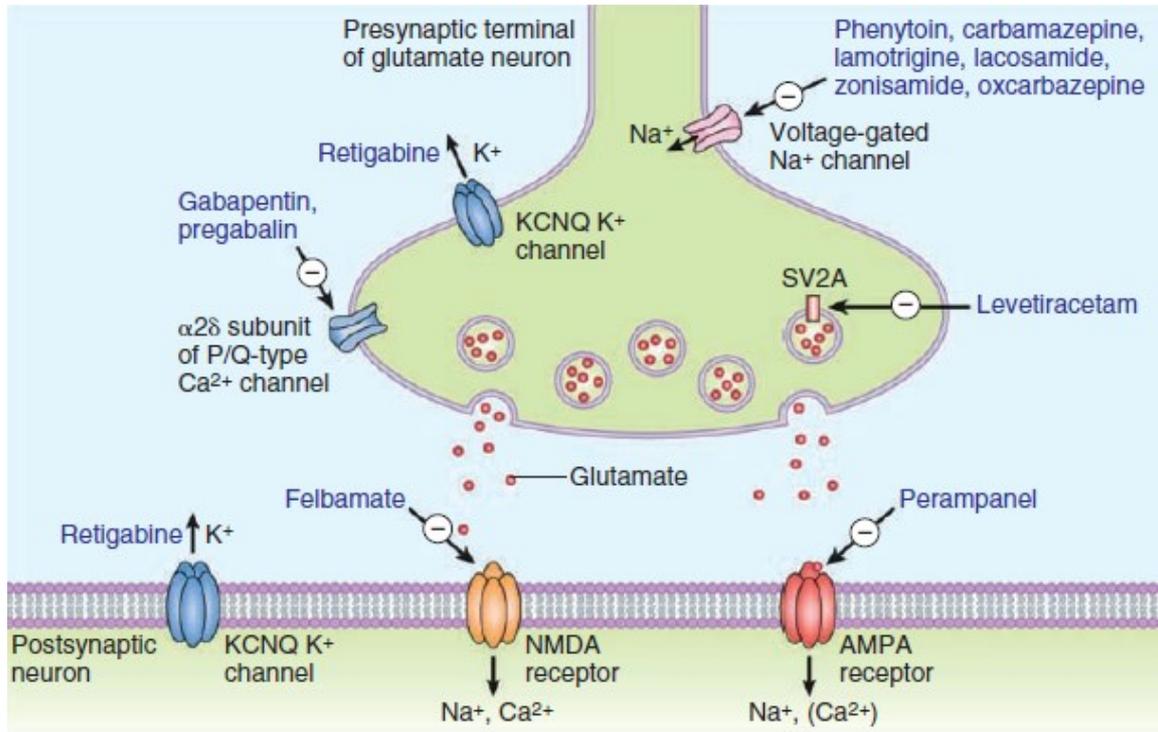






# MOA of antiepileptic drugs

- **Gabapentin and pregabalin**



**TABLE 24–2 Molecular targets of antiseizure drugs.**

Molecular Target	Antiseizure Drugs That Act on Target
<b>Voltage-gated ion channels</b>	
Voltage-gated sodium channels (Na <sub>v</sub> )	Phenytoin, fosphenytoin <sup>1</sup> , carbamazepine, oxcarbazepine <sup>2</sup> , eslicarbazepine acetate <sup>3</sup> , lamotrigine, lacosamide; possibly topiramate, zonisamide, rufinamide
Voltage-gated calcium channels (T-type)	Ethosuximide
Voltage-gated potassium channels (K <sub>v</sub> 7)	Retigabine (ezogabine)
<b>GABA inhibition</b>	
GABA <sub>A</sub> receptors	Phenobarbital, primidone, benzodiazepines including diazepam, lorazepam, and clonazepam; possibly topiramate, felbamate, ezogabine
GAT-1 GABA transporter	Tiagabine
GABA transaminase	Vigabatrin
<b>Synaptic release machinery</b>	
SV2A	Levetiracetam, brivaracetam
α2δ	Gabapentin, gabapentin enacarbil <sup>4</sup> , pregabalin
<b>Ionotropic glutamate receptors</b>	
AMPA receptor	Perampanel
<b>Mixed/unknown</b> <sup>5</sup>	Valproate, felbamate, topiramate, zonisamide, rufinamide, adrenocorticotropin

Fosphenytoin is a prodrug for phenytoin.

Oxcarbazepine serves largely as a prodrug for licarbazepine, mainly *S*-licarbazepine.

Eslicarbazepine acetate is a prodrug for *S*-licarbazepine.

Gabapentin enacarbil is a prodrug for gabapentin.

There is no consensus as to the mechanism of valproate; felbamate, topiramate, zonisamide, and rufinamide may have actions on as yet unidentified targets in addition to those shown in the table.

Modified from Rogawski MA, Löscher W, Rho JM: Mechanisms of action of antiseizure drugs and the ketogenic diet. *Cold Spring Harb Perspect Med* 2016;6:a022780.





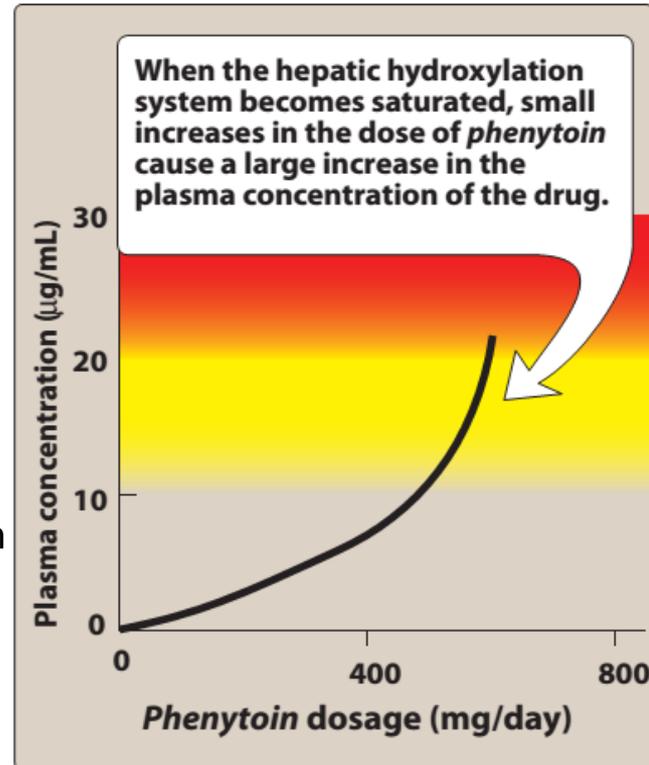




# Phenytoin and fosphenytoin

Self reading...  
P. 418-419

- **Pharmacokinetics**
- **Phenytoin** binds extensively to plasma proteins (97–98%), and free (unbound) phenytoin levels in plasma are increased transiently by drugs that compete for binding (eg, carbamazepine, sulfonamides, valproic acid).
- Phenytoin **induces** drug-metabolizing enzymes.
- Phenytoin exhibits **saturable enzyme metabolism** at a low serum concentration. Therefore, small increases in a daily dose can produce large increases in the plasma concentration, resulting in drug-induced toxicity.





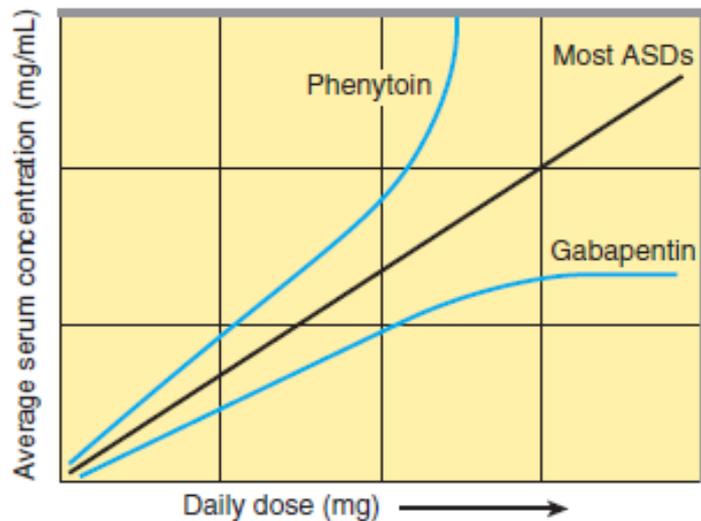












**FIGURE 24-4** Relationship between dose and exposure for antiseizure drugs (ASDs). Most antiseizure drugs follow linear (first-order) kinetics, in which a constant fraction per unit time of the drug is eliminated (elimination is proportional to drug concentration). In the case of phenytoin, as the dose increases, there is saturation of metabolism and a shift from first-order to zero-order kinetics, in which a constant quantity per unit time is metabolized. A small increase in dose can result in a large increase in concentration. Orally administered gabapentin also exhibits zero-order kinetics, but in contrast to phenytoin where metabolism can be saturated, in the case of gabapentin, gut absorption, which is mediated by the large neutral amino acid system L transporter, is susceptible to saturation. The bioavailability of gabapentin falls at high doses as the transporter is saturated so that increases in blood levels do not keep pace with increases in dose.







# Clinical Uses of Antiseizure Drugs

« نضيف »

## A. Generalized Tonic-Clonic Seizures

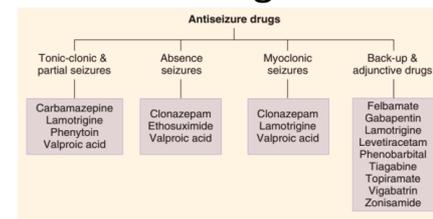
- **Valproic acid, carbamazepine, and phenytoin** are the drugs of choice for generalized tonic-clonic (grand mal) seizures.
- **Phenobarbital** (or primidone) is now considered to be an alternative agent in adults but continues to be a primary drug in **infants**.

## B. Partial Seizures

- The drugs of first choice are **carbamazepine** (or **oxcarbazepine**) or **lamotrigine** or **phenytoin**.

## C. Absence Seizures

- **Ethosuximide** or **valproic acid** are the preferred drugs because they cause minimal sedation.
- **Clonazepam** is effective as an alternative drug but has the disadvantages of causing sedation and tolerance.



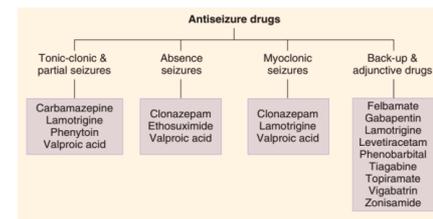
# Clinical Uses of Antiseizure Drugs

## D. Myoclonic Seizure

- Myoclonic seizure syndromes are usually treated with **valproic acid**.
- **Lamotrigine** is approved for adjunctive use, but is commonly used as monotherapy.
- **Clonazepam** can be effective, but the high doses required cause drowsiness.

## E. Status Epilepticus

- Intravenous **diazepam** or **lorazepam** is usually effective in terminating attacks and providing short-term control.
- For prolonged therapy, intravenous **phenytoin** has often been used because it is highly effective and less sedating than benzodiazepines or barbiturates. However, phenytoin may cause cardiotoxicity (perhaps because of its solvent propylene glycol), and **fosphenytoin** (water soluble) is a safer parenteral agent.
- **Phenobarbital** has also been used in status epilepticus, especially in children.





Questions??

