



## Issues for Seniors with Epilepsy

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Seniors (in this article we are considering individuals over 60 years as seniors) have an increased incidence of epilepsy. In individuals between the age of 25 and 50 there are about 25 new cases per 100,000 people per year, but after 50 years the incidence rises with increasing age from 70 per 100,000 per year in the 55 to 60 year group, and 150 per 100,000 after 70 years. In most cases these are partial seizures (which means that they start in one area of the brain) with or without progression to a generalized tonic-clonic seizure. The period of confusion or weakness after the seizure (called the post-ictal state) tends to be longer in the older individual than in younger people. This increased incidence of epilepsy in seniors is due to the increased frequency of brain conditions such as strokes (cerebrovascular accidents) and degenerative diseases of the brain such as Alzheimer's disease with increasing age.

Epilepsy is characterized by the tendency to recurrent seizures. Seizures are a transient alteration in behavior and can appear in many different ways. The BC Epilepsy society website has more information about the different kinds of appearances of seizures. The diagnosis of epilepsy can sometimes be quite challenging in seniors because in this age group people may have spells for other reasons. Some testing and observation may be required to determine if the spells are seizures, TIAs (transient ischemic attacks) or confusional spells due to a dementing illness.

It is easier to make the diagnosis of epilepsy when the first spell is a generalized tonic-clonic seizure (also called a grand mal seizure) with stiffening and loss of consciousness. These patients usually end up the emergency room and get some further testing quickly. A first seizure can be the sign of an underlying brain condition such as a hemorrhage, stroke, or infection that will require immediate treatment. In all cases, it is important to prevent further seizures so an antiepileptic drug (AED) will usually be started immediately. Tests such as CT scan, MRI, EEG, and blood work will look for underlying causes.

If the likelihood of further seizures is considered to be high, then the doctor will prescribe an AED to be taken after leaving the hospital. This medication acts to prevent the abnormal electrical activity in the brain that leads to a clinical seizure. The goal is to be on a medication with minimal side effects that will prevent further such events.

The treatment of epilepsy in seniors presents some unique challenges: Injuries caused by seizures in the elderly may be more severe because their bones and tissues are not as strong. Post-ictal confusion can go on long enough that the person doesn't eat or drink or move for many hours and this is problematic in someone living alone. The loss of driving privileges that result from having a seizure is a serious blow to independence at any age, but it is often not as easy for the elderly to start using public transportation as it might be for younger persons.

There are also age related changes in the way the body handles the antiepileptic medications, and there is a great deal of potential for drug interactions with other medications being taken for blood pressure, hypercholesterolemia and pain. See below for more details with each AED. The seniors are also more sensitive to the side effects of any of the AEDs because of a slowed metabolism and an older brain, and it may take some different trials to determine which drug will work the best for a given individual.

The medication most commonly prescribed for all ages is phenytoin (Dilantin). This drug has the advantage that it can be started in the emergency room, where patients often end up after their first seizure. It can be given in a loading dose, so that it is immediately effective, although it will take 10 days on the daily dose prescribed before the level becomes steady. This drug can lead to poor balance and slowed thinking, particularly when the level is on the higher side of the therapeutic range. It will also often slow function in a patient who has other neurological deficits from brain injury such as a stroke or recent brain surgery. Some patients also complain of slowed cognition and depression on this drug but there are many who feel just fine while taking it.

The most important pathway for drug metabolism among the AEDs is the hepatic cytochrome P450 enzyme system (CYP). The common AEDs: phenytoin, carbamazepine, and phenobarbital (often called the older AEDs because they have been in use for more than 40 years) are all enzyme inducing because they all cause this P450 system in the liver to become more active. Therefore, when a patient is taking any of these three enzyme-inducing AEDs, their other drugs such as some of the cholesterol lowering drugs<sup>1</sup>, or birth control pills, or blood thinners will be cleared out of the body faster. The action of these AEDs also results in the body getting rid of vitamin D faster, and this is one reason that they will increase osteoporosis in sensitive patients. When a patient is taking multiple medications, it is very important to ask the pharmacist or doctor about what important interactions may be occurring, and find out what modifications are required.

Another issue is the absorption in the stomach of multiple medications taken simultaneously. Calcium, which is widely taken to prevent osteoporosis, will considerably impair the absorption of phenytoin when taken at the same time, so has to be separated from it by some hours, or the phenytoin levels will be variable and often too low to prevent seizures.

There are several other AEDs for treatment of epilepsy in seniors, which can be used if phenytoin is not working or causing unacceptable side effects.

Carbamazepine is quite similar to phenytoin with many of the same problems associated with its hepatic enzyme inducing properties. It has to be started quite slowly as patients will become dizzy if it is started at full dose suddenly. Some patients seem to have less cognitive slowing and balance with this drug than phenytoin, so if it is started slowly (usually not considered on an emergency room visit) it will be a reasonable choice. Also the side effects of this medication are of much shorter duration than phenytoin, as it does not last as long in the system. This can make their diagnosis easier and the dosage can be adjusted based on how the patient feels.

Phenobarbital is also effective for stopping seizures and very long acting so can be taken once per day. The sedating effect when taken at night may be helpful for patients with anxiety or insomnia. However it also causes other medications to be less effective, and increases osteoporosis, and can affect balance and cognition at higher doses so is not usually used in the elderly. It is least expensive of all the AEDs and still used widely outside of North America and Europe, where it may be the only drug a patient can afford.

Valproate (Epival) is also effective for the elderly and usually well tolerated. But it is more effective for generalized than partial seizures and these are less common in seniors. It is not an enzyme inducing medication but does have some drug interactions due to protein binding. Most important visible side effect in senior is aggravation of preexisting tremor or the new appearance of intention tremor, but this disappears when the drug is stopped.

Gabapentin (Neurotin) is an AED that is widely prescribed for pain in seniors, and is valued because it is excreted through the kidneys and not the liver, so has very little interaction with other medications.

However, it is a weak AED and at doses high enough to stop seizures it may make older patients too drowsy.

Lamotrigine (Lamictal) is one of the newer AEDs that is metabolized in the liver by other pathways and does not have much interaction with other medications and it does not cause osteoporosis. It is not sedating and may sometimes even cause insomnia. It has to be started quite slowly and carefully monitored initially because of a risk of allergic skin reactions in nearly 10% elderly patients<sup>2</sup>. Consequently it is not used very often but is one of the recommended drugs for the elderly in the more recent literature<sup>3</sup>.

Clobazam (Fresium) is a mild AED with few interactions, but may cause sedation and diminished balance in susceptible patients and enhanced effect of other CNS depressants such as alcohol.

Topiramate (topamax), oxcarbamazepine (Trileptal) and levetiracetam (Keppra) are three more of the newer AEDs that may have a place in treatment of seizures in the elderly. They are all quite expensive compared to the ones discussed above. Topamax is an enzyme inducer but effective at low doses. Oxcarbamazepine does not induce the common enzyme pathway so have fewer interactions. Levetiracetam, has the advantage of being excreted through the kidneys like gabapentin and thus has no interactions with other medications. It can also be started rapidly and is usually well tolerated, but in a few patients leads to increased irritability. The experience with using this drug alone for seizure control is still limited. It requires special approval from BC Pharmacare and can only be approved if a patient has failed to tolerate a few of the more common AEDs.

In summary, epilepsy in seniors is a common and challenging condition to treat. The unique issues for this age group are:

1. Diagnosis: there are many spells that appear in the elderly that are not seizures.
2. The elderly get more injuries during seizures because their bones and tissues are not as strong as those of younger people.
3. The commonly used AEDs interact with many of the other medications that seniors are taking. This may make the other medications less effective and/or increase the side effects of the AED.
4. Seniors' metabolism is reduced so the AEDs are clearly more slowly and dosage adjustments may be required.
5. Seniors' brain is more sensitive to the side effects of the AEDs if there are other conditions causing impairment.

Footnotes:

1. These are the statins or HMG-CoA reductase inhibitors class of medications. This interaction lowers the effectiveness of all of these except for Rosuvastatin (Crestor) is the only one in this class not affected by phenytoin.
2. Product monograph for monotherapy in elderly individuals.

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