+ Module Three: Treatment of Epilepsy
Module Three: Objectives

Upon completion of Module Three the participant will:

■ Describe the main treatment options for epilepsy
■ Identify factors essential in the selection of appropriate medications for epilepsy
■ Review the indications for epilepsy surgery
■ Discuss the benefits of dietary therapy for epilepsy
Individuals with Epilepsy have a variety of options when it comes to treatment. Medications are the first option made available. Surgical procedures and implantable devices are also options that are considered if medications are not effective or cause unacceptable side effects.

Dietary therapies provide another avenue for treatment in some patients. While some epilepsy centers may offer these when medications are not effective, others try dietary therapies earlier in the course of treatment or together with medication therapy.
The recurrence rate of untreated patients having another seizure is small. Treatment is usually recommended after a first seizure in patients with abnormalities in the brain or with abnormal EEGs and a familial history of epilepsy. The goal is to attempt to control seizures with one drug and have the least amount of side effects.

About 60% of people who new onset seizures will respond to the first one or two drugs tried. Of the remaining 40%, a small percent will respond to the next few drugs, but the rate of response or seizure control declines markedly after the first few AEDs tried, assuming that the AEDs were the appropriate drug for the patient’s seizure type and was tried at the correct dose for an adequate length of time.

References:

The ultimate goal of treatment is help the person become seizure free without side effects of medications or other treatments. For some people this may be easy to achieve. For others it may be quite difficult or not within reach with treatments currently available. Nevertheless, there have been many advances in epilepsy treatment in recent years such that people should not settle for continued seizures without first exploring all appropriate treatment options.
Antiepileptic Medications (AED)

- Good oral absorption and bioavailability
- Most metabolized in liver but some excreted unchanged in kidneys
- 1st generation AEDs generally have more severe CNS sedation than newer drugs
- Drugs chosen based on mechanism of action, side effect profile, and impact on comorbid conditions, i.e. migraine, depression
- Add-on therapy is used when a single drug does not completely control seizures

There are many available AEDS, with the majority of older AEDs metabolized by the liver. These ‘older’ AEDS are thought of as the 1st generation of seizure medications. They tend to have more side effects, including cognitive and sedating effects, many of which may worsen in relation to dose.

While the goal is to treat the patient with monotherapy or one drug to minimize side effects and drug interactions, for many patients this isn’t possible. When adding another AED, choosing drugs with different mechanisms of action may be preferable or choosing medicines that will complement each other, in terms of how they work, drug interactions, and adverse effects.

The choice of medication treatment will depend first on having an accurate diagnosis of the type of epilepsy. The type of medication prescribed will also depend on several factors specific to each patient, such as tolerability of side effects, comorbid states, and acceptable delivery method of medications. Cost of medications also play an important role and can become a concern regarding compliance, if the patient is unable to afford the drug.
Certain forms of epilepsy are more likely to respond to treatment better than others.

The list above captures the ideal components for medications to achieve the goal of controlling the seizures with minimal side effects.

The intravenous route allows for treatment to continue in the event that the individual has seizures that are nonstop and cannot take medication by mouth, or needs to get the level of the medication absorbed quickly.

Reference:
For about 70 percent of those people diagnosed with epilepsy, seizures can be controlled with medications.

People with epilepsy may take medicine up to four times a day to prevent seizures. Drugs for epilepsy treat the related symptoms. They do not cure the disease.

There are many different forms of epilepsy, and certain types of medications seem to work best for different types of epilepsy.

References:


Medication compliance or adherence in the past has been promoted as one of the main causes of breakthrough seizures. Research into this area has highlighted those at greatest risk of adherence problems, for example people who take medications 3 or more times per day, and those with complex medication regimes. Interestingly, it has been suggested that people with well-controlled epilepsy may have more problems with taking medications than those with poorly controlled epilepsy. Other factors, including attitudes and beliefs about seizures and medications, knowledge, and behaviors play important roles in understanding medication adherence.

Medication compliance infers that patients must do what the doctor orders. However, using a self-management perspective, this definition doesn’t take into consideration the myriad of patient-specific factors that influence medication-taking. Thus the term adherence or medication-taking behaviors is the preferred terminology from the nursing perspective.
Pharmacokinetics is the action of drugs in the body over a period of time or what the body does to the drug.

**Absorption** is the first step and pertains to how long it takes for the medicine to be absorbed into the bloodstream. Factors influencing absorption rates may include how the drug is ingested and whether an oral dose is taken on an empty stomach or after food; different medicines may have different rates of absorption; and some concomitant medications, such as antacids for example, can affect the absorption of some AEDs.
Metabolism and elimination are critical pharmacokinetic properties to understand. These processes describe how drugs are broken down or metabolized in the body and excreted. Many seizure medications are metabolized in the liver and excreted. Drugs can also be excreted in the feces, through the lungs, the skin, and through the breast.

Impaired kidney function can cause a buildup of drug and active metabolites and will increase toxicity and prolong the duration of drug action.

The term bioavailability refers to how much drug gets into the brain to work as intended. This may vary among different drugs depending on a number of factors.
Drug concentration is the amount of drug measured in a given amount of plasma or blood. The loading dose is determined by volume of distribution of drug and weight of the patient. The maintenance dose is determined by rate of elimination of the drug. Whether or not a loading dose is needed depends on the reason for starting the medication and acuity of the patient’s status at the time. For example, a patient who has had a cluster of seizures, or is in the midst of a seizure emergency may need a loading dose of a medicine to reach a desired level quickly. This can’t be done with all medicines however. If a person is starting a drug for routine care, the medicine may be started and increased slowly over a number of weeks.
Blood levels of an AED may be used as a guide in determining response to treatment, but this information should be considered along with the patient’s self-report of seizures and side effects, as well as clinical examinations.

Additional laboratory monitoring is important, but the type of tests needed and frequency of monitoring will depend on the specific medication.
All of these things are considered at one time or another with the patient that is treated with AED medication. Individuals that demonstrate sound self management skills can actively participate in discussion with their clinicians and care givers on all of these topics.
General Instructions

- Patients must take medications as prescribed on a daily basis to maintain a therapeutic blood level to prevent seizures.

- Patients should not abruptly stop medications – raises risk for seizure emergencies.

- Factors that can influence how the drug gets into the body, works in the body, and is metabolized and eliminated can interfere with the serum blood drug levels and interact with other medications.

Stopping epilepsy medication without a doctor's guidance is one of the major reasons people who have been seizure-free have breakthrough seizures. Seizures that result from suddenly stopping treatment can be serious and can lead to status epilepticus. Furthermore, there is some evidence that uncontrolled seizures trigger changes in the brain that can make it more difficult to treat seizures in the future.

The odds of successfully stopping epilepsy medication are not as good for:

- People with a family history of the condition
- Those who need multiple medications
- People with focal seizures
- Those who continue to have abnormal electroencephalogram (EEG) results while on medication.
There are many different drugs available to treat seizures and epilepsy. Some of the more effective medicines, such as phenobarbital and Dilantin have been around the longest. Unfortunately, they also have many unacceptable side effects. The term ‘2nd generation’ AEDs include those that have been approved since the early 1990’s. The following two slides show the drugs that fall into 1st and 2nd generation categories.
Above are examples of 1st generation AEDs

- 1857- Bromides
- 1912- Phenobarbital
- 1938- Phenytoin (Dilantin)
- 1954- Primidone
- 1960- Ethosuximide (Zarontin)
- 1974- Carbamazepine (Tegretol)
- 1975- Clonazepam (Klonopin)
- 1978- Valproate (Depakote)
Of the newer AEDs, now called 2nd generation drugs, the efficacy is at least equal to the older agents. Many possess a broad spectrum of activity and can be used for treatment of different types of epilepsy. While many were initially approved by the Food and Drug Administration as add-on therapy, some are also used as a single treatment or as monotherapy. The second generator medications appear to be safer and better tolerated by patients. Since fewer of the AEDs are metabolized by the liver, protein binding and drug interactions are not as problematic as some of the older medications. Less monitoring of liver function tests or other metabolic parameters are suggested as well.
The chemicals in generic drugs are exactly the same as in the brand-name drugs, but they may be absorbed or processed differently in the body because of the way they are prepared.

Patients should always check with their doctors before switching to a generic version (but staying with the same generic house whenever possible).
Different seizure medicines tend to yield different types of side effects. Just because a certain effect is common with one medication, however, does not mean that the individual will experience it. Many people have few or no problems with side effect.
Some side effects are associated with specific medications and occur fairly frequently. Examples of some idiosyncratic effects are listed here. Of note, these will vary from one drug to another.

Common dose dependent side effects are usually related to symptoms of the central nervous system and occur with higher dose amounts.

Allergic reactions, such as rash or anaphylaxis may occur with any drug.

Nurses should be aware of all types of side effects for commonly used AEDs. It’s critical to recognize that side effects can be unpredictable, just like seizures, and contribute to intolerance of a medication.
Stevens-Johnson Syndrome is a life threatening skin condition in which cell death causes the epidermis layer of the skin to separate from the dermis. The syndrome is thought to be a hypersensitivity complex that affects the skin and the mucous membranes. It is critical that nurses, patients and their families are aware of the potential for this and other serious adverse effects and know what to do if symptoms should arise.
Drug interactions are common with many of the older seizure medications and some of the newer ones. A seizure medication can interact with another seizure medication affecting how well either one works or altering the metabolism and concentration of the drug. The interaction, for example, may speed up or slow down how quickly a medication is eliminated, either making it less effective at preventing seizures because a lower level is present in the blood, or more likely to build up to toxic levels and cause side effects. Other prescribed medications or over the counter medications could affect some seizure medications and the opposite can occur as well. People who are taking other non-seizure medications should review these medicines carefully with their nurses and doctors. The selection of an AED and the extent of monitoring required will vary depending upon the potential for drug interactions.
Rescue medications used to stop seizures in progress exist for use by both medical and non-medical personnel.

For trained medical personnel, as well as caregivers in the home, rescue medications are used to stop prolonged seizures in the emergency room.

Various rescue medications exist:
- Rectal diazepam gel
- Tablets, liquid, sublingual: lorazepam
- Tablets: diazepam
- Tablets/wafers/disintegrating tablets: clonazepam
- Intranasal: midazolam (not approved yet)

Expand on when to give and why individualized protocol, examples
Patients who have rescue medications prescribed will need careful teaching about when, how, and in what circumstances to use rescue medicines. If a patient is hospitalized, the plans for rescue medicines may change, depending upon the patient’s seizures, reason for admission, and methods of drug administration preferred during the hospitalization.
Epilepsy 101: Getting Started

When Seizures Do Not Respond to AEDs

- Patients whose seizures are not controlled after 2 or more trials of appropriate medications should be referred to the next level of care for appropriate evaluation and treatment. For example,
  - Refer to a neurologist if seizures persist after 3 months of care by a primary care provider
  - Refer to an epilepsy specialist if seizures persist despite treatment with general neurologist for 12 months

For about 30% of people with epilepsy, seizures do not respond to standard medical therapy. When side effects are considered, even more people report that AEDs do not work or are not tolerated. Based on research and recommendations of the International League Against Epilepsy and the National Association of Epilepsy Centers, the following criteria are generally used to determine when seizures do not respond to AEDs.

Patients whose seizures are not controlled after 2 or more trials of appropriate medications (chosen for their seizure type and used at appropriate dose for appropriate length of time) should be referred to the next level of care for evaluation and treatment.

People should be referred to a neurologist if seizures persist after 3 months of care by a primary care provider.

Referral to an epilepsy specialist should be considered if seizures persist despite treatment with a general neurologist for 12 months.

There are always exceptions to these criteria. For example, people whose seizures are difficult to diagnose may need to be referred to an epilepsy center sooner in their care to determine if they are having seizures. People with devastating or progressive forms of epilepsy should also be considered for referral early so that comprehensive care can be provided and more specialized evaluations and treatment addressed.

References:
When antiepileptic drugs fail to control seizures, surgery to control may be considered. Although some of the techniques are recent, surgical removal of seizure-producing areas of the brain has been an accepted form of treatment for more than 50 years. Most surgical patients are adults who have fought long and unsuccessful battles for seizure control.

Discuss disabling seizures and how affects quality of life
Specialists in the field of epilepsy look at indications for surgery.

A pre-surgical work up is completed with the patient and family at the forefront of the team. Multiple test are done to determine the location of seizure onset and whether it is coming from one area that can be removed without causing further deficits or problems. Patient and family learning needs, expectations and supports are critical during this work-up and the entire surgical process. Nurses may work with patients in various settings during a surgical evaluation- on an inpatient epilepsy monitoring unit, epilepsy or neurology clinic, primary care or community-based settings.
There are multiple types of surgery options; depending on identification of seizure focus. The most common type of surgery is a resection of the seizure focus, most commonly in the temporal lobes (ie. temporal lobectomy). Outcomes will vary depending on individual patient characteristics, location of seizure focus, type of surgery, and comorbid conditions for example. However, epilepsy surgery in appropriate candidates can offer freedom from disabling seizures in 60 to 90% of people. Before having surgery, extensive testing and discussions about benefits, risks and appropriate expectations are conducted among the epilepsy team, the patient and their family or support network.

Reference:
VNS therapy is a device that is able to help control seizures in some patients. It is approved for use in patients who are not candidates for epilepsy surgery or who have failed to respond to surgery. It consists of a generator which is surgically placed under the skin on the left side of the chest and an electrode that is attached to the vagus nerve in the left side of the neck. The generator and electrode are connected under the skin. While we don’t know fully how vagus nerve stimulation work, the device sends bursts of electrical stimulation to activate the vagus nerve which then stimulates the brain. The stimulation parameters are set by a programmer, usually a doctor or nurse, usually for 30 seconds every 5 minutes. The stimulation can be varied to deliver more or less frequent stimulation. VNS Therapy is not a cure for epilepsy, but is an additional treatment that can help control seizures in some people.

References:

Epilepsy Patient’s Manual for Vagus Nerve Stimulation with the VNS Therapy System. Houston, TX, Cyberonics, Inc. www.cyberonics.com


Additionally, the patient can activate the stimulation at the time of a seizure by swiping the magnet over the generator in the left chest. For many people, this magnet stimulation can help abort or lessen the intensity of seizures. This is used as part of seizure first aid. The magnet can be used by the patient, family, observer or anyone trained on how to use it.

The VNS magnet can also be used to stop bothersome side effects or turn the stimulation off temporarily at any time. This is done by holding or taping the magnet over the generator.
Dietary therapy is used to treat refractory epilepsy and has been around since the 1920’s. The classic ketogenic diet is the most restrictive of the three diets and is based on a ratio of 4 grams of fat to 1 gram of protein and carbohydrates. Using dietary therapy for epilepsy, particularly the ketogenic diet, requires a dietician. Most centers initiate the KD during an inpatient stay. The MAD and LGIT diets are less restrictive and do not require an inpatient stay. MAD restricts carbohydrates but allows unlimited proteins and fats. The LGIT is based on low glycemic foods.

References:


Dietary Therapies
Indications and General Tips

- For people with refractory epilepsy, when medications don’t work or are not tolerable
- May allow reduction in AEDs if seizures can be controlled.
- Ketogenic diet is the most restrictive, may require a hospitalization and few days of fasting to start it. Difficult for older children and adults to tolerate
- Modified Atkins and Low Glycemic diets are less restrictive and easier to tolerate by many people

Dietary therapy is an adjunctive treatment that can be very helpful for children and adults who do not respond to medications. When the diet works, AEDs may be lowered to lessen side effects in some people. The ketogenic diet is the most restrictive and difficult to use for many, especially adults. However, advances in different diet treatments have increased their ease of use. People using dietary treatments should first be seen by an epilepsy specialist skilled in dietary therapy, ideally with a nutritionist and nurse for proper education and monitoring.