



## Beating Bad Seizures, Part 2 of 3

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In last month's article, I talked about what epilepsy is and how it is diagnosed. I talked about different kinds of seizures and the importance of careful seizure observation. Most epilepsy diagnoses in children are based upon the parents' observation of what happens during seizures. Unfortunately few parents are taught exactly what to observe or what the various types of seizures look like. Healthcare in the U.S. is not set up to spend hours educating each parent. That puts everyone at a disadvantage. If the parents cannot provide a full and accurate description, the doctor is less able to make an accurate diagnosis. Since effective treatment often depends upon an accurate diagnosis, the result can be poorly controlled seizures despite competent attempts at treatment. For some of you, the brief description of seizure types and seizure observation in last month's article will be enough to make a dramatic difference in your child's care. For others, the suggestion of videotaping your child's seizures may make the difference you are seeking.

However, a correct diagnosis is just the foundation of successful treatment. We have to build upon that foundation with appropriate therapy that is carried out accurately. Many believe that the doctor carries out the treatment, but that is not true. The doctor prescribes treatment. Parents have to carry it out day by day. The success in treatment is absolutely dependent upon how accurately you, the parent, apply the treatment each and every day. Unfortunately training in treatment techniques for parents is as rare as training in diagnostic techniques. That puts you and your child at a disadvantage. The Seizures & Epilepsy Education (S.E.E.) program was designed as a part of the UCLA Comprehensive Epilepsy Program to fill these gaps in parent education and to provide parents and others with effective coping skills for the psychological, family, and social challenges of epilepsy. Epilepsy specialty centers have sponsored S.E.E. programs and doctors have prescribed S.E.E. to help their patients get better treatment outcomes. Remember, knowledge is power – and seizure control. In this article, I will share with you the treatment options available for difficult to control seizures and, possibly more important, some of the things you should know to carry out the daily treatment of your child successfully.

### THE TREATMENT OF EPILEPSY

Once a diagnosis is made, treatment must be planned. There are a few types of epilepsy known as “*benign epilepsy*.” These are specific kinds of epilepsy known to involve only few seizures or are known to eventually go away on their own. About 10 percent of epilepsy is benign. Most children will have a kind of epilepsy that requires treatment.

It may not sound like great comfort, but if your child is going to have epilepsy, now is the time for it. Never have there been so many treatment options. And never have advances in epilepsy care come so rapidly. You and your doctor have access to an unprecedented range of methods to achieve seizure control.

Since the dawn of time, there have been four revolutions in epilepsy treatment. There is a fifth revolution on the horizon. Each revolution represents a new and different way of controlling seizures. Each has an important place in the modern treatment of epilepsy.

## Lifestyle

The first revolution in epilepsy treatment was lifestyle management. Back in the days before medications for seizures were discovered, the only real way people had to treat epilepsy was to live a lifestyle that reduced the chance of seizures. Certain behaviors were discovered to make seizures more likely. Certain lifestyle adjustments made seizures less likely to occur.

Every human being has what is known as a “*seizure threshold*.” The seizure threshold is the amount of biological stress our brains can take before it has a seizure. All people and animals are capable of having a seizure if their seizure threshold is exceeded. The threshold is interesting because its level changes with changes inside our bodies and sometimes with changes in our surrounding environment. While changes in the seizure threshold are not particularly important to people who do not have epilepsy, for people with epilepsy these changes can mean the difference between having seizures and being seizure free.

Several things are known to lower the seizure threshold. Possibly the most important “*seizure trigger*” is sleep deprivation. Many of you are already familiar with this. Your child needs to get the amount of sleep he or she needs to be fully rested. That could be as little as six hours and as many as ten hours, depending on the child. Fatigue and physical exhaustion can lower the seizure threshold. This does not mean your child cannot go out for sports – it only means he or she needs to train and condition properly. Proper physical exercise raises the seizure threshold, making seizures less likely. Mental activity also raises the seizure threshold. Thus, letting your child become a couch potato may put your child at risk of seizures for a couple of reasons. My particular beliefs about seizure triggers can be found in [Figure 1](#). Since there is not enough research about situations that lower seizure threshold, your doctor’s opinion may differ from what you see here. At the least, these are things to watch for. A good seizure diary will tell you which of these things might affect your child.

Stress is universally believed to cause seizures – with little scientific evidence. There is some research that suggests stress may have a protective effect against developing epilepsy in animals. On the other hand, there is some research suggesting that relaxation techniques, yoga, and biofeedback for stress may reduce seizure frequency. Stress is a part of everyday life and you should not attempt to shield your child from it. If you do, your child will not develop adequate skills to handle stress, a problem that will plague him or her throughout life. Instead, children need challenges that include stress. But make sure that under stressful situations your child gets enough sleep. I suspect the real culprit in stress is the sleep deprivation. Help your child relax and get a good night’s sleep rather than tossing and turning and going over stressful events in his or her mind for much of the night. Relaxation techniques might help with this.

There are some physical conditions that lower the seizure threshold. These include sleep and fevers. For some children sleep is the only time in the day their threshold is low enough to permit seizures. Many of you have noticed seizures are more likely when your child is ill. Tylenol or Motrin is usually OK for fevers, but check with your physician first. There is also some evidence that allergies may lower seizure threshold. However, care should be taken as antihistamines are known to lower seizure threshold and should probably be avoided in sensitive children. Sometimes flickering lights, certain sounds, or hyperventilation (breathing

hard to the point of dizziness) can bring on seizures, but this is not common. Many more people are unnecessarily afraid of these things than are affected by them. Do not let baseless fears keep your child from going to the movies, playing video games, or competing in sports. Keeping a good seizure diary can help you sort out whether or not something in the child's activities or surroundings actually does make his or her seizures worse.

Girls may have a particular problem with their seizure threshold. When they are old enough to have a monthly period, the changes in hormone levels can affect their seizure threshold. There are two points in the monthly cycle where estrogen (which lowers the threshold) is high and progesterone (which raises the threshold) is low. During these times seizures are much more likely. If your daughter has seizures tied to her monthly cycle, there are some add-on treatments that might be of help. Brief use of Diamox®, certain benzodiazepines (Valium® like medications), and natural progesterone during the monthly cycle have benefited some women.

Diet may affect seizures. Hypoglycemia, or low blood sugar, may lower the seizure threshold. Children should eat a diet that maintains a relatively constant blood sugar level. Sugary snacks can cause blood sugar levels to go up and then come down dramatically. Dieting can also lower sugar levels and may be a problem in teenaged children. Small meals through the day are better than two or three big meals. Your doctor can refer you to a dietician or nutritionist who can help you establish a healthy eating pattern with your child. There is some concern that caffeine may make seizures stronger or last longer.

There is a treatment for seizures that was discovered in ancient times from lifestyle changes. In early Greece it was well known that starving a person with epilepsy often caused them to have dramatically fewer seizures. In the 1920s doctors from the Mayo clinic discovered why this happened, leading to the birth of the "**ketogenic diet.**" When a person is starving, their body uses up all of its stored carbohydrates for energy and starts using stored fat for energy instead. When the body burns fat for energy, a byproduct known as ketones accumulate in the bloodstream. It turns out ketones are antiepileptic. In the ketogenic diet, the body is fooled into thinking it is starving. The child gets almost no carbohydrate in his or her diet and instead gets lots and lots of fat. The body is forced to use fat for energy, and in the process produces ketones. Seizures stop in 20 to 30 percent of children and seizures are reduced by at least half in another 40 to 50 percent. About 20 to 40 percent get no benefit. The diet requires an experienced dietician and absolute cooperation from the child and parents. The diet is difficult to manage and is not the most appetizing. When it works, children and parents are often willing to put up with it. In an interesting development, there is some recent evidence the Atkins diet, which also restricts carbohydrate to some extent, might help raise the seizure threshold. More study is needed about this, though.

## MEDICATION

The second revolution in epilepsy treatment was medications. It started with the use of bromides in the latter 1800s. Effective antiepileptic drug (**AED**) treatment began in 1912 with phenobarbital and 1937 with Dilantin®. In the last ten years the number of major AEDs has doubled from eight to 16, with more on the way. This means you and your doctor have many more choices for getting good seizure control without unreasonable side effects. (See the side panel **Antiepileptic Drugs (AEDs).**)

Using medication to treat epilepsy is not as simple as just taking a pill. Three things must be achieved. First, the **right medication must be chosen** for the kind of seizures your child has. Different medications work best for different seizures. The wrong antiepileptic medication may have no effect and can even make certain kinds of seizures worse! This is why having an accurate diagnosis is so important to successful treatment.

Second, medication needs to be chosen to have the *least amount of side effects* for the child. Here is where the new medications may have an advantage. So far research has not shown the new AEDs are necessarily more effective at stopping seizures than the old drugs, but there is evidence that some have less side effects for some patients. Another important treatment principle is to *use only one medication whenever possible*. Using two or more medications can significantly increase the risk of side effects. It has been estimated that 80 to 90 percent of patients will get the best seizure control on one medication alone. Two medications might be required for particularly difficult cases, and very rarely three. Four antiepileptic medications are not considered good practice according to practice guidelines. Recent research found that while 60% of patients become seizure free on one medication, only 5% became seizure free on two medications, and the chance of becoming seizure free on three or four medications was about one in a thousand each. Meanwhile, side effects from two or especially three or more medications can cause problems with attention, learning, behavior and overall quality of life.

Third, it is not how much you take by mouth that counts; *it is what is in your bloodstream that matters*. I tell a joke in the S.E.E. program for patients and families with epilepsy. “I don’t care if you get up in the morning and have to pour yourself a bowl of Lamictal®, add milk and sliced banana and eat it with a spoon...if that is what you need by mouth to get the right amount in your bloodstream, then that is what you should do!” Obviously this is an exaggeration, but the point is critical. It is what is in your bloodstream that counts. Seizure control (and side effect control) comes with maintaining *exactly the right amount of medication* in your child’s bloodstream *at all times*.

This right amount of medication in the bloodstream is known as the “*therapeutic range*.” I am sure many of you have heard of it. However, there is a lot of misunderstanding about what the therapeutic range is. The lower limit of the therapeutic range is defined by the minimum amount you need to have in your bloodstream to cause a reduction in seizures. The upper limit is the maximum *amount* you can have in your bloodstream before you start having unacceptable side effects from the medication. Notice a key word in this definition: “**you**”! As it turns out, *each and every child has his or her own individual therapeutic range*. Doctors use a “published” therapeutic range as a starting point to come up with an appropriate amount of medication for the child. But the published range is based upon the study of a particular group of people with epilepsy, not your child. The therapeutic range for this group can be, and often is, different from your child’s therapeutic range. **Figure 2** explains how antiepileptic medications behave in the bloodstream. Understanding this is critical to knowing how much of a challenge it is to be sure your child maintains the right concentration in his or her bloodstream at all times.

One of the important parts of epilepsy treatment is learning a person’s individual therapeutic range. This is done through the use of blood tests under specific conditions. This learning can take some time. As the child goes on a medication, the doctor will take blood levels to try to figure out how much your child needs by mouth to get the right level of medication in your child’s bloodstream. To begin with, the doctor will use the published therapeutic range as a guide. At this point it becomes very important to watch how the child reacts to the medication. As the amount of medication is slowly increased and the child starts showing an improvement in seizure control, it is important to get a blood level at the time seizures improve. This will give you and the doctor some idea of what the minimum amount of medication in your child’s bloodstream is required for seizure control.

If your child is still having some seizures, the medication should be increased further – again carefully watching the response. If the child starts having “*toxic*” side effects (have too much medication in his or her bloodstream), another blood level should be taken. This level tells you and the doctor what the maximum amount of a particular medication is for your child. If your child responds well to a medication adjustment with no seizures and no side effects, then another blood level should be taken. This time the level tells you what the ideal amount in your child’s bloodstream might be. By taking blood levels, you and the doctor can eventually learn the therapeutic range for your child. Be sure to write down blood level readings along with

their date, medication dosage, and circumstance (seizures started to reduce, toxic side effects occurring, good control – no side effects) so you can learn along with the doctor what range works for your child. Blood level testing is available for all of the old and new AEDs.

If finding the individual therapeutic range for your child were the only problem, the treatment of epilepsy with medication would be easy. Unfortunately other things in your child's life can affect his or her blood level. One of the biggest problems is forgetting (accidentally or on purpose) to take a dose of medication. Research has shown the leading cause of unnecessary seizures in epilepsy is failure to maintain proper blood levels of antiepileptic medication. Remember, the battle is won or lost in the bloodstream. If you forget a dose, the amount in the bloodstream goes down and "breakthrough" seizures can occur.

If you suddenly stop medications, a more serious problem can occur called "*status epilepticus*." Status epilepticus is the condition of being in a continuous, nonstop seizure or in a series of seizures where the person does not regain full consciousness between seizures. Where regular seizures do not appear to cause lasting harm to your child, status epilepticus can cause harm to the brain and even death. The most common way people being treated for epilepsy go into status is by suddenly stopping their medication. The risk of going into status by stopping medication has been estimated to be only 10 percent, but are you willing to gamble on it? Think of epilepsy as a bottle of soda that is shaken up. The cap on the bottle is your antiepileptic medication. If you suddenly pop the cap off the bottle, what will happen? Except in the extreme case of an allergic reaction, AED doses are slowly reduced (tapered) to protect against causing status epilepticus. Fortunately, outside of suddenly stopping your medications, status epilepticus tends to be rare. You can help protect your child by maintaining those blood levels at all times. A few children with epilepsy have a tendency to go into status epilepticus. They need the most aggressive treatment and may benefit from an additional medication called Diastat®, which is used to stop prolonged seizures or groups of seizures.

Forgetting is not the only challenge. Other medications can affect blood levels of your child's antiepileptic medication as well. Some medications can decrease blood levels, especially other antiepileptic drugs. This is another reason why one drug is preferred to two whenever possible. However, other prescription drugs, certain over the counter medications, and even herbals can reduce blood levels (and seizure thresholds.) It is important for you to ask questions of your doctor and your pharmacist about potential interactions when your child is about to be given another medication or supplement. The opposite can happen as well. Another medication can increase the blood level of an antiepileptic drug. If this happens, your child can become toxic on the medication. Again, ask first.

Report side effects to your doctor, otherwise he or she will not know there is a problem. What are the signs that your child may have too much medication in his or her bloodstream (known as signs of "toxicity")? Ask your doctor *and* pharmacist. They can explain the specific signs to watch for. In general, excessive sleepiness, loss of muscle coordination, irritable behavior, blurred vision, nausea, and memory problems are possible signs of toxicity. Keep in mind that there may be another explanation for these symptoms, such as not enough sleep or behavioral problems not related to the medication. When problems such as these occur, your task is to report them to the doctor and then work with him or her to figure out what is actually causing the difficulty.

Even simple things can affect blood levels. For example, calcium can interfere with the body's ability to absorb Dilantin®, Phenobarbital, Mysoline®, and Gabatril®. In this case sources of calcium should be avoided two hours before and two hours after a medication dose. Grapefruit juice can cause blood levels of some medications like Tegretol®, Carbatrol®, and Trileptal® to go up, possibly causing toxic side effects. Several medications can lose some of their antiepileptic effects when your child becomes toxic on the medication. Do not give extra seizure medication to your child. Not only do you risk toxicity, but an

increase in seizures as well. The bottom line is the therapeutic range is the therapeutic range – you should not go below it or above it.

I hope you are getting the message that the task of maintaining proper blood levels is difficult. It requires close attention and a lot of questions of your doctor and pharmacist. If you have more than one doctor treating your child, you will have to call attention to the possibility of drug interactions whenever new medications are prescribed, even antibiotics. If your antiepileptic medication was chosen properly, and if you succeed in maintaining constant blood levels, you should be rewarded with improved seizure control and few side effects. If you are doing all you should and there are still seizures or side effects, then a change of medication or treatment strategy may be in order.

Antiepileptic drugs have dramatically changed the face of epilepsy for most people. It is usually the first line of defense against seizures and allows most people to eventually gain full control over seizures. However, medications must be managed much more carefully than most parents realize. Some children require trials with several different medications before the best one is found. This takes time and can be frustrating, but stick with it. You and your child could be rewarded with good results. Do not forget to pay attention to lifestyle as well. Lifestyle changes have the advantage of having no bad side effects. For some people proper medication with lifestyle changes can mean freedom from seizures.

## **SURGERY**

The third revolution in epilepsy treatment is surgery. In over half of the people who have epilepsy, seizures start from a specific spot in the brain. This is called a seizure “*focus*.” That focus can be surgically removed, or with a new procedure, surgically isolated from the rest of the brain. One of the most common causes of uncontrolled seizures is a condition known as “*mesial temporal sclerosis*.” It is an abnormality that usually occurs in one temporal lobe. It often can be found with a high resolution MRI scan. If your child has it, research suggests there is only about a 10 percent chance that medications will control his or her seizures. On the other hand, surgery for seizures caused by mesial temporal sclerosis is reported to have success rates of up to 80 to 90 percent.

Surgery can result in a cure for epilepsy. If the source of seizures is removed, there is no epilepsy (though it is good practice to keep the patient on antiepileptic medications for a year or two after the surgery to make sure it was a success.) It turns out epilepsy surgery is one of the most successful surgical treatments for any kind of medical disorder. Overall success rates can range from 65 to 85 percent or better.

The success of surgery depends upon the success with which the seizure focus is identified: its exact location, exact size, and degree of certainty it is the only source of seizures. While surgical skill is important, it is the skill of the diagnostic team in finding the seizure focus that is critical. As a result, if you are thinking about surgery, go to an epilepsy surgery specialty center that has lots of experience in finding seizure focuses. That is the expertise you want. With a clearly defined focus, the chance of surgical success skyrockets.

Parents have a number of understandable concerns about epilepsy surgery – after all it is brain surgery. It sounds dangerous, but the complication rate is relatively small. Infection and bleeding is probably the most common of these unusual events. Stroke can occur, and rarely death. The neurosurgeon should explain these and any other risks that could be present for your child prior to deciding on surgery. In comparison to the hazards posed to the child by uncontrolled seizures and / or the prospect of multiple medications, the risks of surgery could be quite small.

Parents are also afraid if you cut out part of the brain, the child will lose some mental abilities. By far the most common epilepsy surgery is a “*temporal lobectomy*” (see **Figure 3.**) This is where the surgeon takes out the front portion of the temporal lobe. There are decades of research looking into the consequences of this procedure, and it has little impact upon mental abilities. There could be some reduction in short-term memory and learning, but these abilities are often more impaired by seizures. If the surgery is on the temporal lobe on the left side, the person might have mild difficulty with coming up with the right word they want to use in the middle of a conversation. It is the “its on the tip of my tongue” experience we have all had. This usually improves with time. Temporal lobectomies can sometimes slightly reduce a person’s field of vision, though not enough to interfere with daily life. The epilepsy specialist and neuropsychologist should be able to give you a good idea of whether any of these changes might occur. Epilepsy surgery does not change personality and it does not fix behavioral problems. It only deals with the seizures.

Sometimes the seizure focus is located in a part of the brain that cannot be removed because it would cause an important impairment. Fortunately, this situation is more the exception than the rule. However, there is a new surgical procedure called “*multiple subpial transection*” that isolates the seizure focus from the rest of the brain without removing brain tissue. A recent review of worldwide experience with this procedure found excellent rates of seizure reduction, with 62 to 87 percent of patients having a 95 percent or better reduction in seizures, depending upon seizure type. This opens new prospects for patients who were not surgery candidates before due to the location of their seizure focus in the brain.

There are many parents who are reluctant to make a decision on surgery for the child. They want to wait until the child is old enough to help decide whether or not to have surgery. That may be a big mistake. Waiting years before surgery means that the child is subjected to years of seizures, years of medications, and years of the disabling impact of epilepsy on development. By the time the child is old enough to help decide, epilepsy has already taken its toll on social, emotional, and academic development. I know it is hard, but my advice to parents is to make the decision as early as possible if medications are not working and surgical treatment is an option. Not only may you stop seizures, but you may also save your child’s development and give your child a better quality of life throughout his or her entire life.

## **BRAIN STIMULATION**

The fourth revolution in epilepsy treatment is brain stimulation. This is the newest treatment revolution. It started in 1997 with the FDA approval of the “*Vagus Nerve Stimulator*” (VNS). Brain stimulation involves the use of small amounts of electricity to stimulate the brain or nerves. The VNS does not directly stimulate the brain, but stimulates the vagus nerve in the neck, which in turn is thought to stimulate the brain indirectly. The VNS has an electrical stimulator a bit larger than a silver dollar that is implanted in the body right below the collarbone. A wire goes from the stimulator to the vagus nerve. The stimulator gives a small amount of electrical stimulation to the nerve for a set amount of time, and then it shuts off for a set amount of time. The doctor can change the length of this on and off cycle and the amount of stimulation given to fit the needs of each patient.

The Vagus Nerve Stimulator is not a silver bullet. According to a summary of the first five years of experience with the VNS after FDA approval, about 56 percent of patients who have the stimulator for a year have a 50 percent reduction in seizures. About 20 percent have a 90 percent reduction in seizures or greater. Few patients become seizure free, though it does happen. What makes these results remarkable is patients getting the VNS have usually failed to respond to medications and are often poor candidates for surgery – in other words they are patients with some of the most difficult to control epilepsy. When you consider how difficult their cases are, the improvements with VNS become more impressive.

There are new brain stimulators in development. These directly stimulate the brain, either on the surface of the brain (the cortex) or deep inside the brain. One of the interesting parts of this research is that some scientists are trying to create what is known as an “intelligent” brain stimulator. Unlike the VNS which has a pre-set on and off cycle, the “intelligent” stimulator detects when the brain is about to have a seizure and stimulates prior to or during the seizure to stop the seizure.

Detecting a seizure before it happens has been a “holy grail” in epilepsy research for decades. Only recently has computing power, miniaturization, and a sophisticated understanding of brain activity *begun* to allow for the creation of devices that can sometimes detect pre-seizure brain activity. I think this is an extremely exciting development. Even if direct brain stimulation does not work (though like everything else in epilepsy treatment, I think it will work for some people and not others), the possibility of being able to predict seizures before they occur is extremely important. How happy would people be to have a small implant near their ear that would beep some minutes prior to a possible seizure? Would having a warning in advance be helpful to you? Such a device does not yet exist, but I see it on the horizon. As I said in the beginning of this series, this is a very exciting time for epilepsy treatment.

## GENE THERAPY

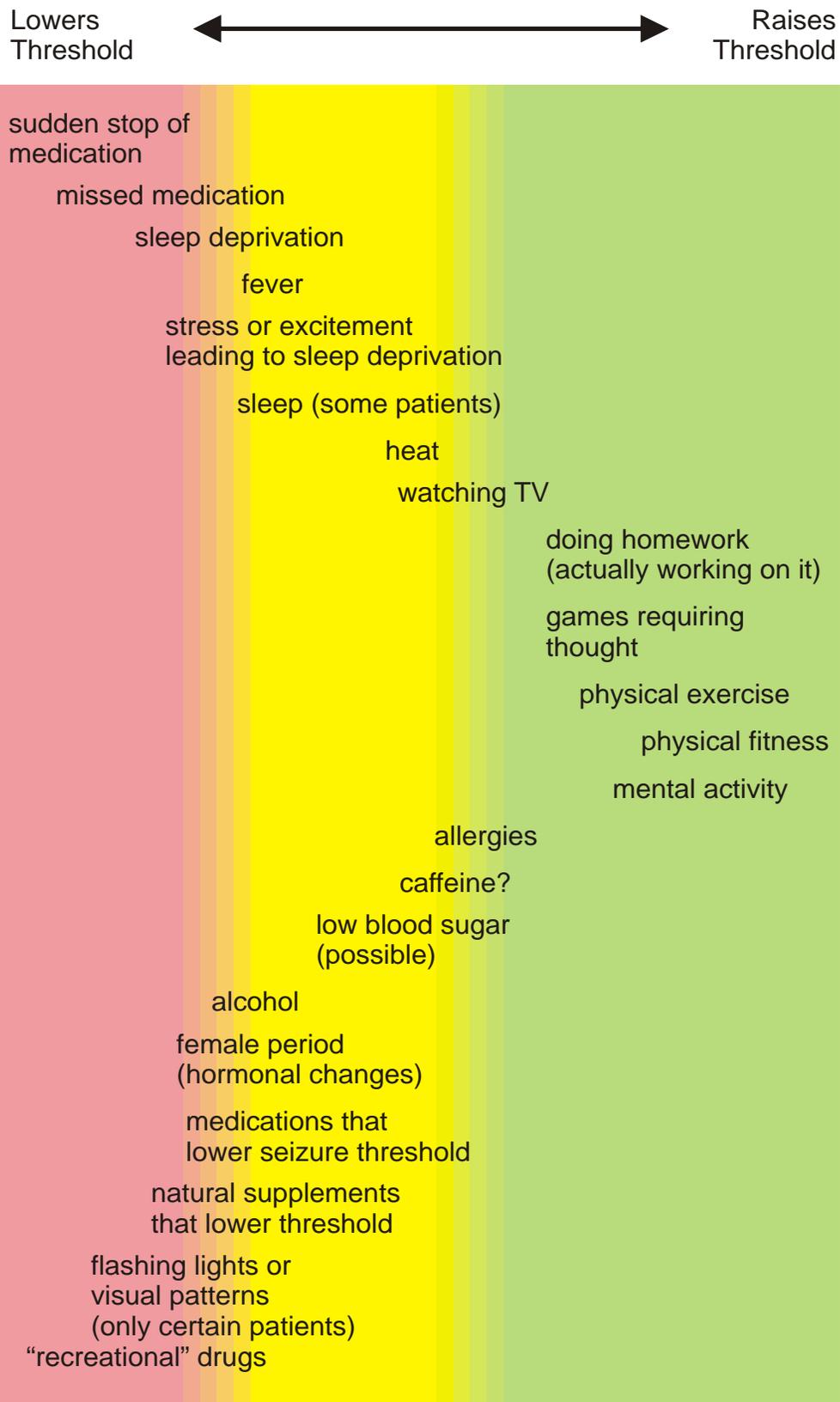
The fifth revolution in epilepsy treatment has not happened yet. The fifth revolution is gene therapy for epilepsy. The first tests of this approach are just beginning in animals. Right now researchers are investigating placing a gene for an antiepileptic protein into brain cells of mice using a virus. Other researchers are beginning to understand the genetic basis to some kinds of human epilepsy. Certain genetic variations in the way brain cells work may appear related to the risk of epilepsy. Researchers are trying to understand how these variations work to make epilepsy more likely. There appears to be an incredible number of genetic variations that can contribute to epilepsy. To get an idea of how many variations there can be – and to get an idea of how incredibly far researchers have gone in studying the genetics of epilepsy, take a look at **Figure 4**.

The results of genetic research could be monumental. Benefits could include the ability to intentionally design medications to compensate for genetic problems in order to control seizures, the use of genetic testing to aid in the selection of the most effective medication for a particular person, and the possible development of genetic treatments like the one being tested in mice. ***All of this is in the future.*** It is not here now. But advances have been so incredibly fast paced that some of these things might come to be in the not-too-distant future.

Now you know about the four basic treatment options and about a fifth approach that is on the horizon. You know how to get the most from each treatment option. You understand both the challenges and the careful attention required to treat seizures with medications. From the first article in this series you know what epilepsy is and how it is diagnosed. You know how you can make a difference through your ability to observe and record your child’s seizures carefully. In the next and final article about the medical aspects of epilepsy, we are going to put this all this information together and use it to give your child the best chance for seizure control. The goal is no seizures and no side effects.

# Figure 1

## Lifestyle Activities that May Affect Seizure Threshold



## Side Panel 4: Antiepileptic Drugs (AEDs)

| <b>Brand Name</b>   | <b>Chemical Name</b> | <b>Published Therapeutic Range<sup>1</sup></b> | <b>Thought to be useful for<sup>2</sup></b>    | <b>Most common side effects<sup>3</sup></b>   |
|---------------------|----------------------|--|--|---|
| (various)           | phenobarbital        | U.S. 14-40<br>Canada 50-130                    | <b>GTC, SPS, CPS, 2GEN, MCS</b>                | Behavioral changes, irritability, restlessness, hyperactivity, drowsiness, impaired attention                                   |
| Dilantin, Phenytek  | phenytoin            | U.S. 10-20<br>Canada 12-80                     | <b>SPS, CPS, 2GEN, GTC</b>                     | Nausea, headaches, tremor, sedation, cognitive impairment, gum growth, osteoporosis, ataxia (loss of muscle coordination)       |
| Mysoline            | primidone            | U.S. 5-12<br>Canada 25-50                      | <b>GTC, CPS</b>                                | Behavioral changes, irritability, restlessness, hyperactivity, drowsiness, impaired attention                                   |
| Zarontin            | ethosuximide         | U.S. 40-100<br>Canada 300-700                  | <b>ABS, MCS</b>                                | Anorexia, nausea, cramps, abdominal pain, weight loss, diarrhea, hiccups, irritability, ataxia                                  |
| Diastat             | diazepam             | Used no more than five times per month         | <b>SPS, CPS, 2GEN, MCS</b>                     | Sleepiness, diarrhea, dizziness, ataxia, rash   |
| Tegretol, Carbatrol | carbamazepine        | U.S. 4-12<br>Canada 12-50                      | <b>SPS, CPS, 2GEN, GTC</b>                     | Nausea, sleepiness, fatigue, dizziness, double vision, incoordination, headache, diarrhea                                       |
| Klonopin            | clonazepam           | U.S. 20-80<br>Canada 60-220                    | <b>CPS, MCS, L-G</b>                           | Sleepiness, ataxia, behavior problems, dizziness, depression, irritability, aggressive behavior                                 |
| Depakote            | valproate            | U.S. 40-120<br>Canada 300-600                  | <b>ABS, GTC, MCS, CPS, JME</b>                 | Nausea, headaches, weakness, vomiting, weakness, tremor, dizziness, abdominal pain  |
| Tranxene            | clorazepate          | U.S. 1-2<br>Canada no data                     | <b>CPS, MCS</b>                                | Sleepiness, ataxia, behavior problems, dizziness, depression, irritability, aggressive behavior                                 |
| Felbatol            | felbamate            | U.S. 30-100<br>Canada 200-400                  | <b>SPS, CPS, 2GEN, L-G, IS, ABS, MCS</b>       | Anorexia, sleepiness, infection, vomiting, fever, insomnia, nervousness, may cause weight loss                                  |
| Neurontin           | gabapentin           | U.S. 4-20<br>Canada 40-120                     | <b>SPS, CPS, 2GEN, GTC</b>                     | Sleepiness, dizziness, ataxia, fatigue, tremor, double vision, incoordination, weight gain                                      |
| Lamictal            | lamotrigine          | U.S. 4-20<br>Canada 10-60                      | <b>SPS, CPS, L-G, 2GEN, GTC, MCS, ABS, JME</b> | Dizziness, headache, double vision, ataxia, nausea, blurred vision, sleepiness, rash  |
| Topamax             | topiramate           | U.S. 20-50<br>Canada 10-60                     | <b>SPS, CPS, 2GEN, ABS, GTC, MCS, L-G</b>      | Fatigue, dizziness, ataxia, speech disorders, nausea, weight loss, sleepiness, nervousness, memory problems, cognitive problems |
| Gabapril            | tiagabine            | U.S. 100-300<br>Canada no data                 | <b>SPS, CPS, 2GEN</b>                          | Dizziness, lack energy, sleepiness, nausea, nervousness, tremor, diarrhea, vomiting   |
| Keppra              | levetiracetam        | U.S. 5-40<br>Canada no data                    | <b>CPS, 2GEN</b>                               | Sleepiness, behavioral disturbance, infection, dizziness,   |
| Trileptal           | oxcarbazepine        | U.S. 12-35<br>Canada 30-140                    | <b>SPS, CPS, 2GEN</b>                          | Dizziness, nausea, fatigue, sleepiness, vomiting, double vision, ataxia, behavioral/mood change                                 |
| Zonegran            | zonisamide           | U.S. 20-40<br>Canada 35-200                    | <b>ABS, GTC, L-G, CPS, 2GEN</b>                | Drowsiness, dizziness, anorexia, agitation, irritability, nausea, impaired concentration  |
| Sabril              | vigabatrin           | Does not apply                                 | <b>IS, CPS</b>                                 | Irreversible visual defect, drowsiness, fatigue, headache, dizziness, weight gain, agitation                                    |

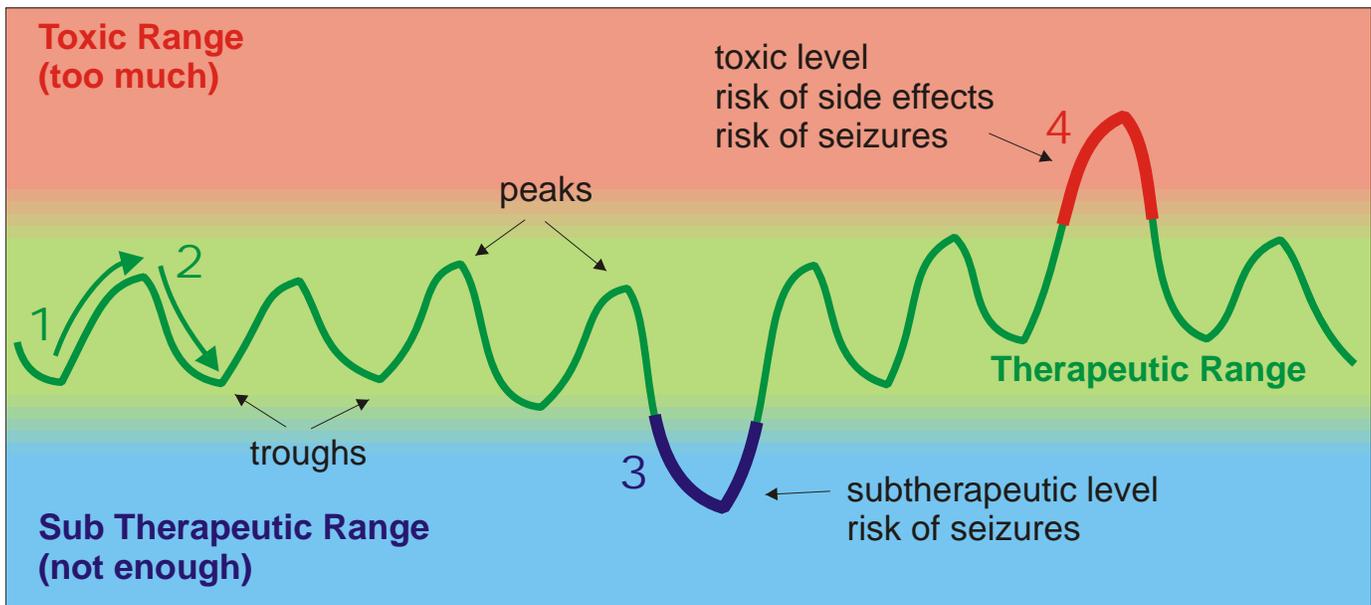
<sup>1</sup> Canada (and other countries) measures blood levels in a different way than the U.S. Canada directly measures concentration. U.S. indirectly measures concentration by measuring the weight of the drug in a certain amount of blood.

<sup>2</sup> Seizure types in **bold** are the ones that the medication is thought most useful for. The medication may be helpful for the other seizure types listed. **ABS** = Absence, **GTC** = Generalized Tonic-Clonic, **MCS** = Myoclonic Seizures (including drop attacks), **IS** = Infantile Spasms, **L-G** = Lennox-Gastaut, **JME** = Juvenile Myoclonic Epilepsy, **SPS** = Simple Partial Seizures, **CPC** = Complex Partial Seizures, **2GEN** = Secondarily Generalized Seizures.

<sup>3</sup> Not a complete list of side effects. Most people only experience a few of the side effects listed. Many do not experience persistent side effects. Side effects tend to reduce as the child becomes accustomed to a medication. It is important to speak with your doctor and pharmacist about side effects and signs of toxicity when starting a medication. Taking more than one medication can increase the risk of side effects.

## Figure 2

# How Medications Behave in Your Child's Bloodstream



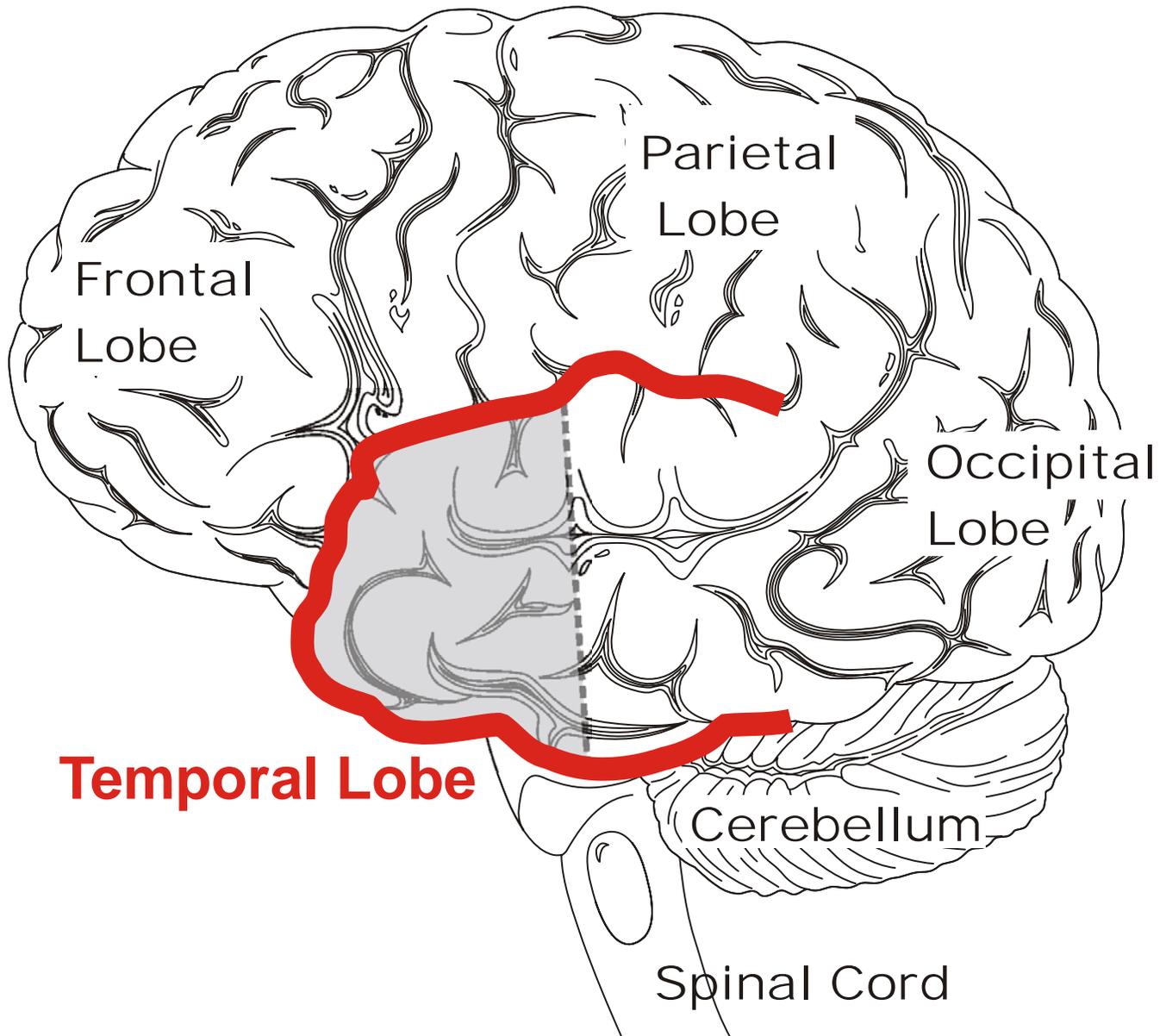
This graph shows the “**therapeutic range**.” The therapeutic range appears in green. The blue area is the “**subtherapeutic range**,” meaning there is not enough medication in your child’s bloodstream to protect against seizures. The red area is the “**toxic range**.” This is when there is too much medication in your child’s bloodstream. You will notice that one range shades into another - there is not a clear dividing line between them. Also notice the amount of medication in your child’s bloodstream is constantly changing.

1. Right after a dose, the amount in your child’s bloodstream increases as the body absorbs the medication. Eventually the amount increases until it reaches a “**peak**” (high point) usually one to four hours after a dose.
2. In between doses, the body slowly removes the medication, so the amount in the bloodstream drops until it reaches a “**trough**” (low point) right before your child takes the next dose. If your child does not take a dose when it is due, the amount in the bloodstream continues to drop. If you child took no further medication, the body would eventually remove all of it from the bloodstream. To use medications successfully, both the “peaks” and the “troughs” have to stay inside the therapeutic range. You can see this is not easy to do. You have to pay close attention to taking the right amount of medication and to taking doses on time.
3. At this point a dose of medication was forgotten, or the prescribed dose was not large enough. As a result, the level of medication in the bloodstream dropped far enough that your child is at risk of having seizures.
4. This is what happens when too much medication is taken - either the prescribed dose was too high or by taking extra doses. The amount in the bloodstream rises to the point where the “peak” is in the toxic range. At the least, this may mean toxic side effects. At the most it could mean seizures. Several of the antiepileptic drugs lose their protective ability when your child becomes toxic on them.

## Figure 3

# Anterior Temporal Lobectomy

Left Side of Brain

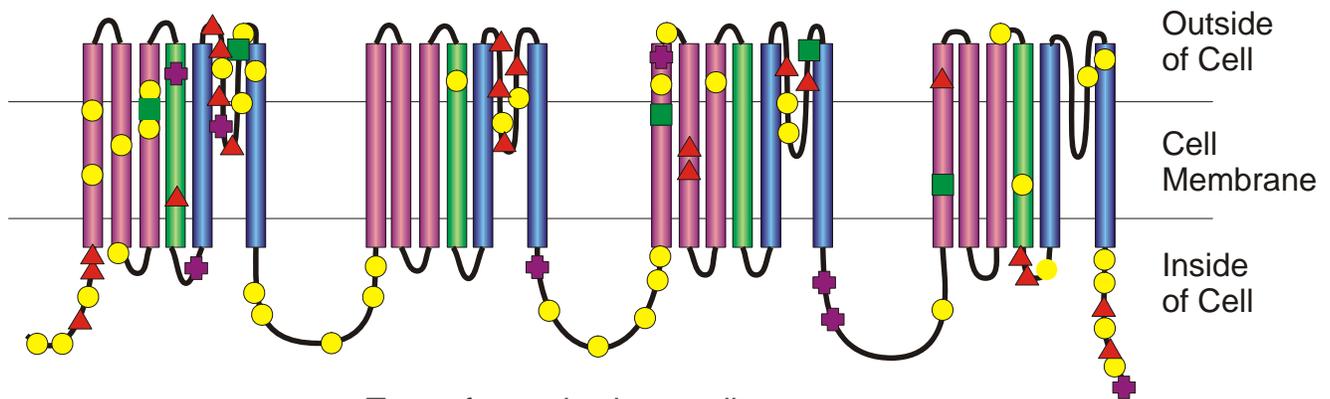


Removal of the front portion of the temporal lobe, the most common type of surgery for epilepsy.

Figure 4

# Different Genetic Abnormalities in a Brain Cell Which Can Cause Just One Type of Epilepsy

This is a diagram of an **ion channel**  
(a sort of pore between the outside and inside of a brain cell  
that the brain cell uses to create and control its electricity)



Type of genetic abnormality

▲ part missing    ■ extra part    ● section missing    ■ wrong shape

**Notice how many different genetic abnormalities can contribute to epilepsy!**