Frequently Asked Questions by Parents of Children with Rasmussen’s Encephalitis (RE)

Introduction

This report has been written by parents and relatives of children with Rasmussen’s encephalitis (RE). Although our battles with RE have been different, we have all known the heartache of having a healthy child who develops seizures and, eventually, physical and cognitive problems. And each of us has had to make extraordinarily difficult decisions about things that are foreign and frightening to us.

The Frequently Asked Questions (FAQ) addresses some of the questions we are asked by parents of a child diagnosed with Rasmussen’s encephalitis (RE), or who doctors have indicated might have RE.

We have answered the questions as directly and honestly as we can. The purpose of this information is not to tell you what decisions you should be making about your child’s treatment, but rather to inform you about your choices and the decisions you face. While we are not doctors we have known dozens of RE patients and read about many other cases, and can offer our opinion on general issues, based on our experience and knowledge. However, we cannot give you specific medical advice. All RE patients are different and decision-making must take into account many complex factors.

What causes RE?

The short answer is we don't know. There is evidence that autoimmune processes cause the damage to brain cells. However, it is not yet clear whether RE is basically a disease of the autoimmune system or whether the autoimmune problem is caused by a virus or other pathogen.

RE is a sporadic disease – it has not been associated with particular environments or populations, and cannot be caught from other people. There is no evidence that RE is inherited, although the possibility that genetic factors predispose people to the disease cannot be ruled out.
The RE Children’s Project has commissioned several research projects directed at finding the cause of Rasmussen's encephalitis.

**How can we be sure it is RE?**

Rasmussen’s encephalitis is a rare disease that causes inflammation of the brain. The disease is nearly always confined to one side (hemisphere) of the brain, either the left or the right. While RE rarely, if ever, spreads to the opposite hemisphere, it progressively inflames areas of the affected hemisphere until all or most of the hemisphere has been destroyed.

RE is a confounding disease, unfolding in different patterns and severity. Most patients are aged between six and ten years when the disease strikes, but younger children, adolescents and young adults can also develop RE.

The hallmark of RE is usually the onset of unexplained seizures in a previously normal individual. The early seizures are often focal, partial seizures, but other seizure types including tonic clonic (grand mal) seizures are also possible. A focal seizure does not cause the child to completely lose consciousness, and affects only a limited part of the body or causes specific sensory or emotional symptoms. It may be difficult to recognise that the child is actually having a seizure.

Most patients develop a variety of seizure types over time. A continuous motor seizure called epilepsia partialis continua (EPC) develops in many patients: this is a form of seizure activity in which a body part, usually a limb, does not stop seizing (twitching). The presence of EPC is strongly suggestive of RE.

RE can progress quickly, with severe and frequent seizures that lead to disability in a matter of months (‘fast burners’) or the disease can progress slowly over a period of years, sometimes with periods of respite (‘slow burners’). Younger patients, especially those younger than five years, tend to be fast burners, and older children and adolescents generally progress more slowly. However, these patterns do not always hold true. And unfortunately, initially slow burning cases of RE can turn into fast burners and will usually also develop very severe and frequent seizures at some stage.

Apart from the patient’s symptoms, the diagnosis of RE can usually be made on the basis of serial EEG and MRI test results. Sometimes, a brain biopsy will be suggested to confirm the diagnosis. You may wish to consider getting a second opinion if this is the case, as a brain biopsy is an invasive operation and the diagnosis is often made without it. Brain biopsies are also often inconclusive as brain tissue affected by RE can sit alongside healthy brain tissue.
Parents who would like to learn about the specific diagnostic criteria should read the 2005 European consensus statement on RE\(^1\) and discuss this with your child's doctor. This paper is available from the RE Children’s Project website, www.rechidrens.org.

It can take some time to establish a diagnosis, as there are a couple of other conditions that can look like RE in the early stages. However, the European consensus statement notes that nearly all cases of RE can be distinguished from other possible diseases within a year of the first symptoms. If your doctor has mentioned the possibility of RE, but said we need to 'wait and see', our view is that you should not wait more than a few months before getting a second opinion. It is important that this second opinion is sought from a paediatric neurologist who has previous experience in treating RE patients.

There are two main types of treatment for RE; medical and surgical. In its early stages most children will be treated with a range of medications, usually anti-epileptic medications and steroids and often intravenous immunoglobulin (IVIG). Another paper by The RE Children’s Project has an overview of current medical treatments.\(^2\) The main ones are noted in the box on page 6 of this paper.

There is no accepted medical treatment regime for RE, and management of the disease varies greatly between clinicians and hospitals. This puts patients’ families in the position of having to inform themselves about the options available so they can discuss these with their doctors.

While medical treatments may help control symptoms and slow the progression of the disease, only a radical surgical procedure, known as a hemispherectomy, offers an end to the seizures and ongoing functional and cognitive decline associated with RE. During a hemispherectomy, the entire affected brain hemisphere is either removed or completely disconnected from the rest of the brain. This is effectively a ‘cure’ for the disease, but one that comes at the cost of inducing disabilities that may not yet have been caused by the disease itself. The answer to our question on ‘life after hemispherectomy’ (page 7) discusses the consequences of the operation.

Occasionally doctors remove a portion of a RE patient’s affected hemisphere (such as the frontal lobe or a smaller section of the brain) instead of removing or disconnecting the whole hemisphere. This is unlikely to be a successful long-term solution because the RE eventually appears in new areas of the hemisphere. We are not aware of any cases where partial removal of the hemisphere successfully stopped the progression of RE.

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Deciding between medical and surgical treatment

The most difficult question facing doctors and parents of RE children is whether, or for how long, to persist with medical therapies in preference to hemispherectomy surgery. The problem with all of the current medical therapies is that they are not effective in the longer term. As we meet more and more RE families we hear the same stories about the drugs and treatments that work for a short period of time, but ultimately prove no match for RE’s unrelenting destruction of the brain hemisphere. To hear this over and over again is heartbreaking.

At The RE Children’s Project research conference in 2010, concern was expressed that approaches used by many centers encouraged delaying surgery until the neurologic deficits become permanent or acceptable to the patient and/or family. This is a real problem because, currently, the best cognitive results occur when the patient stops seizing as early as possible, and this is often before his or her affected hemisphere is consumed by the RE. Long delays before surgery also mean that patients endure many years of seizures, which may impact on them socially, emotionally and cognitively. In addition, rehabilitation and return to life activities are easier for younger patients.

While some hospitals prefer to persist with medical treatments until such time that the functional decline caused by the RE will not be significantly worsened by a hemispherectomy, this is in contrast to the refrain we frequently hear from RE families that have gone through surgery that sooner rather than later is the best approach. The answer to ‘What will happen if my child does not have a hemispherectomy?’ (page 9) provides more information.

It is important to note that adult-onset RE, while extremely rare and devastating, is typically less severe than childhood RE. Hemispherectomy for these patients would be done only as a last resort, because the remaining hemisphere in the adult brain is much less able to take on new functions and so hemispherectomy outcomes are much poorer than in children.

We recognise also that older teenagers with RE in their language dominant hemisphere (usually the left) are in an appallingly difficult situation when it comes to deciding between hemispherectomy and ongoing medical intervention. Speech functions can transfer between hemispheres but the best recovery of language function is if surgery is before age 5 years. While receptive language can transfer until early adolescents, expressive language (the ability to form words) is usually impaired to some extent with surgery after age 7-9 years.
In situations where hemispherectomy is not an option, the choice of medical therapies should be based on the latest evidence about drugs likely to be most effective in reducing seizures and protecting brain functions. RE patients who do not undergo hemispherectomy surgery will need to be treated for many years, so it is also important to consider which therapies will be safest when used for a long time.

*Continued on page 7.*
Common medical (non-surgical) treatments for RE

**Anti-epileptic drugs (AEDs)**
The seizures in RE have limited response to AEDs; EPC is particularly unresponsive. Despite this, patients with RE usually end up taking multiple AEDs, as the right combination of AEDs will sometimes give temporary seizure relief—although often at the expense of considerable side effects. Responses to these drugs, and side effects, are highly individual. Neurology centres at Western hospitals are very experienced in the management of AEDs, so your doctor will be able to advise you on the best choices for your child. Over time the effectiveness of anti-epileptic medication will wane, so it is likely that the mix of medications will need frequent changes.

**Plasmapheresis and immune-absorption**
Therapies that remove circulating antibodies from the blood, such as plasmapheresis and immune-absorption, can be temporarily effective in RE; however, because they have no lasting benefit, they are usually reserved for emergency situations in which there are very severe and frequent seizures.

**Intravenous immunoglobulin**
High dose human immunoglobulin (IVIG), administered for several months or more, may lead to improvements in seizure control and cognition. IVIG is a blood plasma product that attempts to get the patient’s immune system to behave in a more normal way. It has a very good safety profile and presents few health risks to the patient. The effectiveness of IVIG is increased by combining this treatment with steroids.

**Steroids**
Steroids (Prednisolone/Prednisone) are often the first choice of treatment for RE. These drugs, which try to suppress the immune system and reduce inflammation, may be of some benefit in seizure control. Steroids can cause side-effects, particularly if used in high doses and for a long period of time.

**Chemotherapy and transplant rejection drugs**
A range of chemotherapy-like drugs, such as Cytoxan, and transplant rejection drugs, such as Tacrolimus, have also been tried. These therapies have significant side effects and risks, such as increased vulnerability to major infections. As with IVIG and steroids, there is no evidence that these drugs control RE in the longer term.

**Monoclonal antibodies (Rituxan)**
One new immune modifying drug, Rituxan, created excitement a few years ago when an unpublished study involving eight RE patients suggested that the drug reduced seizures, improved cognitive and motor functions, and greatly reduced progression of the disease. And because Rituxan works on specific immune components, rather than the broader immune system, it is safer and more tolerable than chemotherapy and transplant rejection drugs (though still not without the potential for serious side-effects in rare cases). Unfortunately, case reports available since the initial study have not really supported the early promise of Rituxan. While the drug does appear to have helped some patients, others have received no benefit or only short-lived respite from the symptoms of RE.
How safe and effective is the hemispherectomy?

Hemispherectomy is obviously a very major operation. However, the surgery is safe if performed by a skilled and experienced surgeon working in a hospital that has all necessary facilities for the operation and for post-operative care and rehabilitation. Hospitals in developed countries, such as America, Canada, Europe, the United Kingdom and Australia, report very low rates of major complications and death associated with the operation.

Although not everyone wants to learn too much about the details of the surgery, you should be aware that there are different hemispherectomy techniques. One technique is anatomic hemispherectomy, in which the hemisphere is physically removed. However, most surgeons today perform a ‘functional’ hemispherectomy, where the affected hemisphere is left in the skull and attached to blood supply but no longer functions. Functional hemispherectomy carries less risk of blood loss during surgery, and the patient is not likely to develop an asymmetrically shaped skull post-operatively. Within these two approaches to the surgery there are different degrees of aggressiveness as to how much tissue is removed or disconnected.

Regardless of the technique used, cerebral hemispherectomy performed on RE patients has a high success rate in achieving seizure freedom. The rate of seizure freedom after the operation is about 75% to 85%. Not every institution publishes their success rates, but be careful when comparing rates to make sure that they applies to RE cases. A minority of patients continues to have seizures, but these are almost always much less severe and frequent than before the operation.

Unfortunately, although uncommon, seizures can return some months or even years after the operation. This is often because a small fragment of the hemisphere affected by RE has been left intact in the original operation, or the disconnection was incomplete. When this happens, seizure freedom can usually be obtained by another operation. Although distressing, this does not cause the child to have any greater disability than after the first operation.

A hemispherectomy is extremely complex surgery and requires a specialised paediatric neurosurgeon, trained and skilled in the latest techniques. If hemispherectomy is being contemplated for your child, don’t be afraid to ask hard, probing questions about the surgeon and the hospital. How many hemispherectomies has the surgeon performed and over what period? What technique does the surgeon use? What is the rate of major complications? What percentage of the patients achieves seizure freedom? What percentage of patients requires a second ‘re-do’ operation? What support will the hospital provide after the operation, and for how long? The Hemispherectomy Foundation website, at www.hemifoundation.org, provides a comprehensive list of questions you may consider asking your child’s surgeon. There are also several social media outlets where one can connect to RE families to exchange information.
What will my child’s life be like after the hemispherectomy?

By the time children are considered for a hemispherectomy, their quality of life is usually much diminished and a long way from the normal life they enjoyed before RE. Frequent and disabling seizures may have robbed your child of his or her independence and childhood innocence. It is also possible that one side of your child’s body will have begun to weaken, causing problems with mobility and balance.

The goal of hemispherectomy is to make your child seizure free, and there are good odds this will be achieved. Not having to live with frequent, severe and unpredictable seizures and the side-effects from multiple medications will be a huge improvement to your child’s quality of life.

However, seizure freedom will come at a price. Remembering that the recovery and outcomes after a hemispherectomy are unique for each child, some facts you will need to know are outlined below.

**Movement**

All hemispherectomy patients have partial paralysis on the side of the body opposite the brain hemisphere removed or disconnected. This is because the right side of the brain controls the left side of the body and vice versa.

Because children's brains are ‘plastic’, if surgeons remove or disconnect the affected side of the brain, the remaining side takes over many of the functions of the missing side. With appropriate therapy, most children and adolescents are walking again within weeks or months of the operation, albeit with limps of varying severity. Although many need to wear an orthotic support on the weak leg, some younger children learn to walk and even run without support. Outcomes, however, will vary person to person.

Patients rarely get back much use of their opposite arm and hand; younger children may have some overall arm movement, but fine finger movements are not possible. In all cases, a one handed life is the outcome of the surgery. This is probably the biggest ‘price’ of hemispherectomy, as adapting to life as a one handed person in a two handed world is a major challenge.
Vision

Hemispherectomy patients have a visual field cut (partial blindness) on one side of both eyes. This is permanent, but patients usually adapt to it quite quickly. The visual deficit is not noticeable to other people, and does not impact greatly on the patient’s functioning in everyday life. It will however, affect school work and other tasks that require transferring and reading data. Driving a car is for most is out of the question, although one patient we know has a licence to drive a modified car.

Speech

In most right-handed people, the left side of the brain is responsible for speech. If the left side of the brain is removed, patients will have speech problems immediately after the operation and, depending on their age, may always have some language difficulties. The return of speech following left or dominant hemisphere surgery can be unpredictable in teenagers.

Cognition, social adjustment and overall quality of life

In most cases, RE hemispherectomy patients no longer depend on multiple medications after the operation, and are better able to learn and have more normal social lives. Patients have the same memories and personality as they had before the surgery, although there may be temporary behavioural and mood disturbances after the surgery. Children who have a right hemispherectomy will often be very flat or non-emotive for several weeks or months following the surgery.

The Hemispherectomy Foundation website has many inspiring stories about RE patients who are getting on with their lives following hemispherectomy. Some children adapt so well that they can run, swim, play sports, ride bicycles and dance. A blog post by the mother of one hemispherectomy patient describes the achievements of her daughter and others in the RE community who have had the surgery:

“Abby swims, is in girl scouts, and plays tennis. She walks, runs, climbs, jumps, twirls, and skips. Jessie can ride her bike without training wheels. Robert had his right hemi when he was 11, and has finished his bachelor's degree at the University and now is working on his Master's degree in social work. Jodi can do a ponytail with one hand. Christina can drive a car and also finished her Master's degree in speech therapy so she can help children.”

Sadly, not every story is a good news story, and every patient will experience at least some specific cognitive and other problems, and have varying degrees of difficulty adjusting to life after hemispherectomy. Patients who have a right hemispherectomy often struggle with maths and spatial concepts and some social skills, whereas left hemispherectomy patients can have ongoing difficulty with speech, reading and other language related tasks.
**Success factors**

The extent to which physical, cognitive and verbal functions are regained following hemispherectomy depends on the ability of the remaining hemisphere to take over these functions. This in turn depends on:

- The child’s age. Younger children usually have a better recovery than pre-teens and teenagers.
- Whether the ‘good’ (non-affected) hemisphere was damaged by seizures, drugs or other factors before the operation.
- Whether the operation is able to completely stop the seizures.

The quality of the formal rehabilitation program is also important, especially in the first months following surgery. Further down the track, it is essential that patients are encouraged to remain physically active, as a sedentary lifestyle will lead to weight gain, reduced mobility, and possibly other problems such as reduced self-esteem.

Patients’ emotional and social adjustment to life after hemispherectomy surgery will depend on their personality and the support they receive from family, friends, teachers and health professionals. Where older children and adolescents are involved, it is important that they understand and accept the need for surgery and are well prepared for it. Some patients require counselling and/or medication to help them deal with the emotional adjustment to life after the surgery.

**What will happen if my child does not have a hemispherectomy?**

Every so often we are asked what would happen if a child with RE does not have a hemispherectomy. While every case of RE will progress differently, there is no question that permanent cognitive decline, hemiplegia (weakness to one side of the body) and hemiparesis (paralysis of one side of the body) will occur. If the patient’s dominant hemisphere is affected, he or she will eventually develop speech problems, and may lose the ability to speak.

These problems are similar to those induced by the hemispherectomy itself. However, the important difference is that patients who don’t have a hemispherectomy will have ongoing seizures and cognitive decline, and there will be little opportunity for the good hemisphere to take over the functions of the hemisphere affected by RE. Many patients also develop serious behavioural and psychiatric disturbances as the disease spread to parts of the brain responsible for behaviour and emotion.

Please go to [http://rechildrens.org/images/wordpress/uploads/WarnerPoster1.pdf](http://rechildrens.org/images/wordpress/uploads/WarnerPoster1.pdf) to read about a patient who received a more limited resection rather than a hemispherectomy. Had the patient had a hemispherectomy as a child, it is likely that she would be living a relatively normal life instead of facing a life of seizures and slow, ongoing loss of her physical and cognitive abilities.
While the parental decision to have a child undergo a hemispherectomy is a desperate one, it is important to understand that RE children who have a hemispherectomy usually do much better than those who don’t.

As we discussed on page 4, these considerations don’t apply to adult-onset RE, as in these cases a hemispherectomy may lead to worse outcomes than the disease itself.

**Will a non-surgical cure be discovered soon?**

The mission of the RE Children’s Project is to find a real cure for the disease so we can do away with the need for hemispherectomy surgery.

However, we do not want to give false hope to RE patients and their families, and we definitely do not encourage families to refuse hemispherectomy surgery in the hope that a better option will be found soon.

While we have commissioned some exciting research projects, the reality is that progress in curing diseases is often very slow. At this stage we don’t even know the cause of RE and, even if we did, there is no guarantee that this would translate immediately into a cure or even an effective treatment.

All indications are that RE is a complex disease. The many millions of research dollars devoted to other complex diseases, such as Multiple Sclerosis and Parkinson’s, have led to more effective treatments rather than cures, and the treatments themselves have risks and drawbacks.

It is possible there will be a Eureka moment when we identify a dramatic and tolerable cure that stops RE in its tracks. This would be fantastic, but it is more likely that research will lead to gradual improvements in the treatment options. One day non-surgical treatments will offer an acceptable alternative to surgery, but we are not there yet and there and we don’t know when we will be.

**Where can we go to get more information and support?**

Given the rarity of RE, you may feel very alone in confronting this disease. But while we are not large in number, there are still many families that have experienced this tragedy committed to supporting others who are dealing with RE.
The RE Children’s Project aims to ensure that RE families are well informed and connected throughout their child’s illness. We encourage you to familiarise yourself with the materials available through the RE Children’s Project website, at www.rechildrens.org.

The Hemispherectomy Foundation, at www.hemifoundation.org, established by another RE family, has many stories of children who have undergone hemispherectomy surgery. An online support group of families impacted by hemispherectomy surgery will be able respond to any question you may have, often with their own personal experiences.

The paediatric centre where your child is a patient should be able to put you in contact with local community service organisations that support families of children with additional needs.

If your child is having hemispherectomy surgery, the rehabilitation service will employ specialist occupational, physical and speech therapists who will be involved in your child’s recovery. Sometimes these services are located within the hospital, but often a child will be transferred to a specialist rehabilitation centre once medically stable after surgery.

Rehabilitation centres will also be able to put you in touch with local community organisations once your child is home again, and may also offer help with your child’s transition back to school.