FOR PEOPLE WITH DRUG-RESISTANT EPILEPSY:
WHAT'S NEW IN THE 2023 GUIDELINES?

BACKGROUND

Most people with epilepsy have seizures that can be controlled with anti-seizure drugs. However, **1 in 3 people with epilepsy continue to have seizures despite taking medication**. This is known as drug-resistant epilepsy. In 2016, a task force supported by Critical Care Services Ontario released a series of guidelines for the care and management of people with drug-resistant epilepsy who are not candidates for epilepsy surgery, or who choose not to have surgery. These guidelines were updated in 2023.

This handout highlights some of the key updates to the 2016 recommendations and is based on current evidence. If you have drug-resistant epilepsy, the information in these guidelines can help you, your caregivers and your health care providers to make informed decisions about your treatment. Options include diet therapy, drug therapy, immune therapy, or brain and nerve stimulation.

1. KETOGENIC DIET THERAPY

The ketogenic diet is a **high fat, low carbohydrate** diet that can effectively treat seizures in children and adults. This therapy is a medical treatment that must be guided by a health care professional. **Types of diet therapy** include the following:

Classic ketogenic diet (KD)

- Around 90% of calories are from fat. Diet components are weighed/measured and daily calorie intake is controlled.
- The common 4:1 ratio classic ketogenic diet contains 4 grams of fat for every 1 gram of protein and carbohydrate combined.
- Started while in hospital. Can be provided through food or formula by tube feeding or by mouth, or a combination of food and formula.

Modified Atkin's Diet (MAD)

- Less restrictive dietary treatment for older children and adults that can be started at home.
- Carbohydrates are limited, but there is no calorie, protein, fat or fluid restriction.
- Fat intake from food is not defined but rather encouraged.

Medium Chain Triglyceride (MCT) Diet

- Medium-chain triglycerides, delivered as an oil, are the main sources of fat in this diet.
- The addition of MCT oil means less total fat is needed and more carbohydrates are allowed. This can make the MCT diet more palatable than the classic KD.
- MCT oil can be given as coconut oil or as an emulsion, and should be included in all meals when used.

Low Glycemic Index Treatment (LGIT)

- The glycemic index (GI) refers to the effect a food has on blood sugar levels after being consumed.
- Foods that cause blood sugar levels to rise more slowly have a lower GI value.
- The LGIT allows a more liberal amount of carbohydrate, but the diet is restricted to carbohydrates with a GI of less than 50.
- Smaller increases in blood glucose, or less variability in glucose levels, may have anti-seizure effects.

- All treatments must be medically supervised. A full assessment, including bloodwork, is required to ensure that diet therapy is right for you or your child.
- The most common side effects of KD therapy are gastrointestinal symptoms, including vomiting, constipation, diarrhea and abdominal pain.
- It is essential to take multivitamin supplements while on the KD.
- Diet therapy for epilepsy can be used safely in the adult and adolescent populations.
- Diet therapy can also be used in infants with West syndrome, Ohtahara syndrome, epilepsy of infancy with migrating seizures, and infants with focal seizures awaiting epilepsy surgery.

2. CANNABIS

Increasing evidence suggests that medical cannabis may be an effective treatment for some types of epilepsy. Cannabidiol (CBD) and delta-9-tetrahydrocannabinol (THC) are two of the principal components of the *Cannabis sativa* plant. Much of the research on cannabis and seizures in the last two decades has focused on CBD.

Although there are no official Health Canada recommendations nor approvals for the treatment of seizures with cannabis, recent studies have shown that CBD may be an effective treatment for drug-resistant childhood-onset epilepsies, specifically Dravet syndrome, Lennox-Gastaut syndrome, and tuberous sclerosis complex.

Studies using CBD as an add-on therapy have shown a reduction in seizure frequency for all seizure types, particularly when taken together with the anti-seizure medication clobazam. Formulations available in Ontario include purified CBD oils (without THC) and CBD-rich extracts (which contain some THC).

Recommendations:

- **Purified CBD oil may be considered as an add-on treatment** for people who have Dravet Syndrome (DS), Lennox-Gastaut syndrome (LGS) or tuberous sclerosis complex (TSC) and have been diagnosed with drug-resistant epilepsy.

- **An epileptologist should guide the use of CBD oil** in children with LGS, DS, TSC or any other drug-resistant epilepsy. The addition of THC should be guided by a neurologist or epileptologist who has experience prescribing and using medical cannabis in people with epilepsy.

- **Obtaining cannabis for medical use** requires several steps to be taken by both the doctor and the person with epilepsy (or their caregiver).

- Cannabis oil is typically taken twice a day and can be taken with high-fat foods to increase absorption. **The recommended dosage will vary** depending on body weight and the formulation of the oil.

- **CBD may interact with anti-seizure medications** and may cause sleepiness, gastrointestinal symptoms, decreased appetite, or changes in liver function. There is a lack of information about the long-term side effects, including any potential effects on fetal development.

- **Cannabis should not be used in individuals with acute psychosis**, and should be used with caution in those with irregular heartbeat or severe cardiovascular, immune, liver or kidney disease.

- Medical cannabis products should be obtained from a **Health Canada licensed producer**.

- It is **illegal to transport any medical cannabis products** (including CBD-containing products) across the Canadian border and into other countries, even if cannabis is legal in those destinations.

3. IMMUNE THERAPY

What is autoimmune epilepsy?

In some cases, the activity of the immune system (the defense network that protects the body from infection and disease) can cause seizures. This type of epilepsy is known as **autoimmune epilepsy (AE)**. If this is the case, medication can be prescribed to adjust the activity of the immune system to help control seizures.

Antibodies are immune proteins that circulate in the blood and normally detect foreign, harmful substances. Antibodies that target the brain may lead to AE. AE is sometimes seen in people who have other autoimmune diseases, cancer, or close family members with an autoimmune disease.

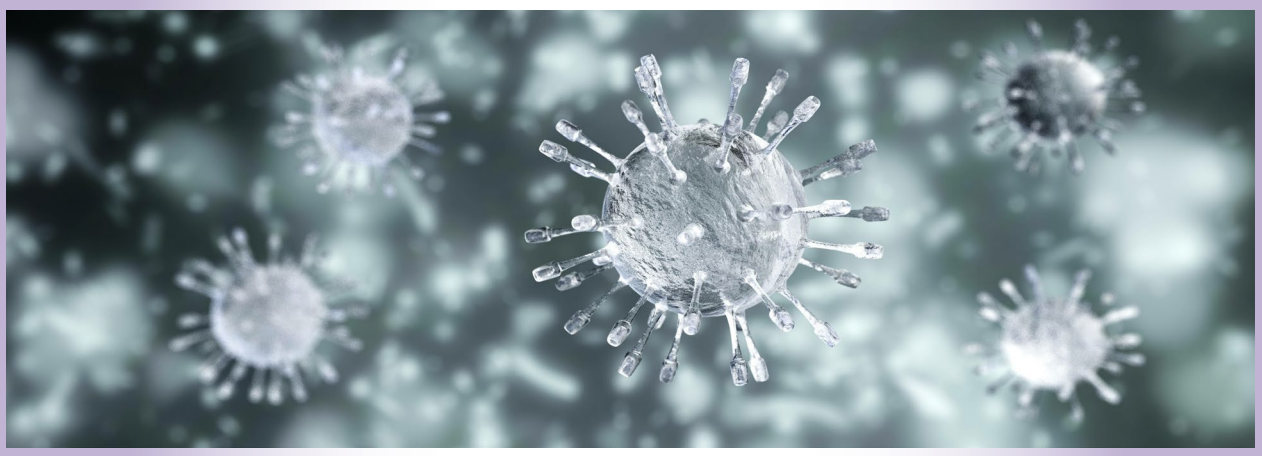
How is it diagnosed?

Health care providers may perform a number of tests to diagnose AE. They will also take a full medical history, look at the type and frequency of seizures, and try to identify where in the brain seizures are starting. They may also perform a lumbar puncture (spinal tap) to look for antibodies in the fluid that surrounds the brain and spinal cord.

How is it treated?

Corticosteroids suppress the activity of the immune system and are one of the main treatment options. These include **methylprednisolone, prednisone or intravenous immunoglobulin (IVIg)**. This treatment approach is used for AE as well as infantile spasms and Rasmussen's encephalitis. People with these conditions often have seizures that are resistant to anti-seizure medications but respond well to medications that decrease immune activity.

Due to the potential long-term side effects of corticosteroids, individuals using corticosteroids are eventually switched over to other types of immune-suppressing medications.

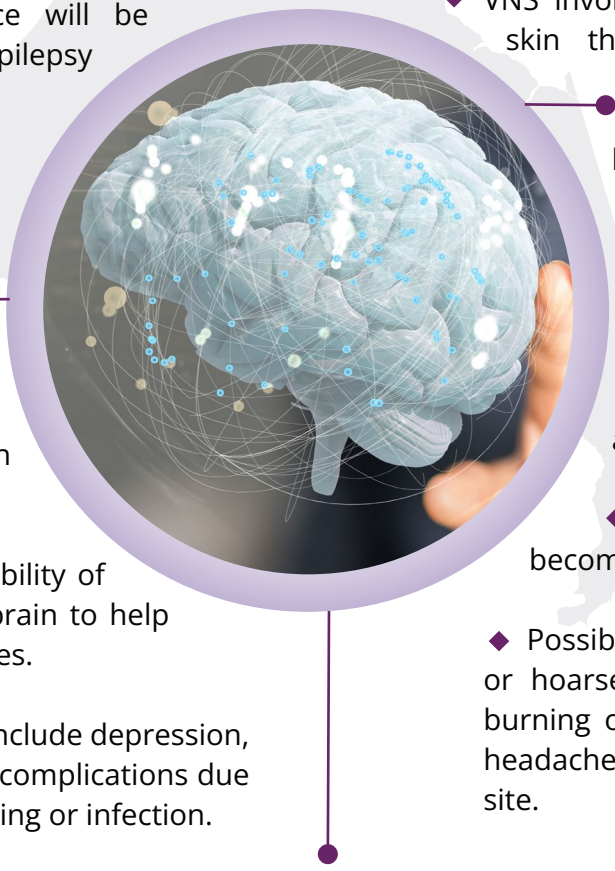


4. BRAIN AND NERVE STIMULATION

For some people, electrical stimulation of specific nerves or brain areas can reduce the risk of seizures. Stimulation may be delivered through devices implanted in the brain or under the skin, or through electrodes placed on the forehead. Since stimulation is less effective than resective surgery, this treatment should only be considered after surgery has been explored as an option.

Deep brain stimulation

- DBS involves implanting electrodes in certain areas of the brain. Once the surgery is complete, the device will be programmed by an epilepsy specialist.
- Stimulation is controlled by a device placed under the skin in the chest. Once the device is turned on, the level of stimulation can be adjusted.
- DBS alters the excitability of particular areas of the brain to help reduce or prevent seizures.
- Possible side effects include depression, memory impairment, or complications due to surgery, such as bleeding or infection.



Vagus nerve stimulation (VNS)

- VNS involves implanting a device under the skin that delivers intermittent electrical stimulation to the vagus nerve (which communicates with the brain) to help reduce seizure activity.
- VNS can be considered for adults and children with focal or generalized epilepsy.
- VNS may also improve mood in adults and children with epilepsy.
- Seizure reduction with VNS can become more effective over time.
- Possible side effects include change in voice or hoarseness, cough, shortness of breath, burning or tingling sensations, nausea, pain, headache and infection at the implantation site.

Other techniques, such as responsive neurostimulation, hippocampal stimulation, external trigeminal nerve stimulation, transcutaneous auricular vagus nerve stimulation and transcranial magnetic stimulation are also being studied. Currently, these techniques are either unavailable in Canada, or there is not enough information to make recommendations about their use in the treatment of epilepsy.

These guidelines are maintained and updated by EpLink – The Epilepsy Research Program of the Ontario Brain Institute (OBI) in partnership with the Epilepsy Implementation Task Force.