Immunotherapy in autoimmune encephalitis

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The purpose of this factsheet is to provide people affected by autoimmune encephalitis, as well as their families and caregivers, information about the specific treatments available for this type of encephalitis. The medications used for autoimmune encephalitis target the immune system and are called immunotherapies.

Patients with autoimmune encephalitis also often require a variety of other medications including antiepileptic drugs (to control seizures), sedatives (to help calm) and anesthetic agents (to control excessive movements or seizures) — this factsheet does not aim to discuss these medications.

General consideration

Every patient is by definition unique, and so are the cause and the effects of the illness on them. Therefore, the specific immunotherapies recommended by the patient's clinician will be based upon each patient's distinctive clinical features (signs, symptoms, and test results). In most forms of autoimmune encephalitis, it is believed that immunotherapies help speed up clinical recovery. However, unfortunately, all medications which target the immune system, may come with potential side effects, especially infections. Patients and their families need to be aware of these effects before they are started on the treatment.

Types of immunotherapies

This section does not provide strict rules, but rather we hope, is an informative and useful resource which can inform you broadly of the relative merits of each drug. The table below is intended to provide a general guide of how and why certain medications may be used, and to outline the benefits and disadvantages of each option.

First-line Therapy – Used initially to treat autoimmune encephalitis

Treatment	Side effects	Why and when is the medication useful?	How is it given?
Corticosteroids (often called 'steroids') e.g., prednisolone or methylprednisolone	Side effects are more likely to happen at higher doses, and after increased durations of treatment. Side effects include problems with acne, thin skin, easy bruising, insomnia, mood swings, muscle weakness (myopathy), high blood pressure (hypertension), changes in appetite/weight, changes in glucose tolerance, weakening of bone (osteoporosis), cataracts, stomach ulcers, and increased risk of infection. In children, reduced growth is a potential complication. Some of these effects are partly opposed by co-administration of drugs, which protect the stomach lining and help prevent weakening of the bones. Rare neurodegenerative and neurotoxic effects (adverse effects) after long-term use If you have been on steroids for a long time, you should not stop them suddenly as you risk serious adverse effects; a slow reduction of steroids should be performed over weeks to months.	Steroids are thought to help increase the speed of recovery, particularly in seizures and memory function. Steroids may help prevention of relapses.	Intravenous infusion for 3-5 days (methylprednisolone) or oral tablet (prednisolone)
Intravenous Immunoglobulins (IVIG)	Side effects include: 1. Flu-like symptoms such as: Headache, cough, dizziness, fatigue & tiredness, nausea, diarrhoea, as well as increased blood pressure, and increased blood clot risk during and for 24 hours after the infusion. 2. As IVIG is derived from pooled (collected) blood from donors, it may contain	When acutely unwell, IVIG may be used to help speed up recovery. More rarely, IVIG is used as a regular treatment.	Intravenous infusion, usually over 5 days. Each infusion takes about 4 hours.

	viruses or unknown infectious agents, which could in theory be passed onto the patients. This is considered to be very rare in practice. 3. Allergic (hypersensitivity) reactions are rare but can occur. They are usually screened for by checking IgA status of patient. Can also develop a reaction at the infusion site.	Often paired with corticosteroid treatment.	
Plasmapheresis or Plasma Exchange (PLEX)	Side effects include: 1. Those relating to the procedure (insertion of the line) such as bleeding and accidental damage to a nearby structure, which may lead to pain. These effects can be minimised by using non-dwelling lines when good vein access is possible. 2. Light-headedness/dizziness (and sometimes fainting), blurry vision, coldness, sweating and tingling in arm during the procedure. The light headedness may be a particular concern when there is a pre-existing problem with blood pressure or heart rate (as seen especially in patients with NMDAR-antibodies). 3. Clotting problems, which can occur as the patient's blood is thinned to minimise risk of clots though this is rare. 4. Rare possibility of an 'allergic' reaction to the plasma. This is monitored for in hospital.	When acutely unwell, PLEX may be used to help speed up recovery. More rarely, PLEX is used as a regular treatment. Often paired with corticosteroid treatment or used as an alternative if patient doesn't respond well to steroid therapy.	Requires a procedure to place a plastic tube into the patient's vein, with aim of removing parts of the blood, and replacing them Each session of plasma exchange lasts 2-4 hours and occurs daily for 5 days or alternate days over 8-12 days.
Second-line Therapy – Used if first-line therapy isn't sufficient enough of a treatment			

Mycofenolate Mofetil (MMF)	Side effects include: 1. Increased risk of infections and bone marrow suppression (see azathioprine). 2. Gastrointestinal upset such as diarrhoea, nausea and more rarely vomiting. These effects can often disappear with time, as the body gets used to the medications. 3. Other effects are very rare: hair loss, acne, gum swelling, high blood sugar, gout, blood pressure changes, blood in urine and vision issues. This medication is not advised during pregnancy.	This medication is usually used when doctors want to gradually reduce the treatment with steroids. It is often described as a 'Steroid sparing agent'. MMF often works in 3-6 months.	Tablet Initially a low dose 2 times a day, which is gradually increased to a higher dose to be maintained.
Azathioprine (AZA)	Side effects include: 1. Increased risk of infections and bone marrow suppression (decrease in some blood cells), as well as an increased risk of cancer. These effects are often carefully monitored in regular blood tests and check-ups. Symptoms of infection or abnormal bleeding/bruising should be reported promptly to the doctor. 2. Liver toxicity. This can cause patients to become sick and appear yellow. Usually this can be reversed by stopping the medication. 3. Pancreatic inflammation (pancreatitis) is a rare complication. 4. Other effects: nausea, vomiting, hives (urticarial), facial swelling, muscle/joint pain, weight loss, hair loss, fatigue or missed periods.	This medication is usually used when doctors want to gradually reduce the ongoing treatment with steroids. It is often described as a 'Steroid sparing agent'. It takes 6-12 months before it starts to work.	Tablet Initially low doses daily, and then gradually increased for 1-2 weeks to higher dose per day to be maintained.

Rituximab	Side effects include: 1. Possible 'allergic' reaction to the medication. Most likely at the site of infusion. This is monitored for in hospital. 2. Increased risk of infections, including cold-like symptoms as a result of the effect of medication of intentionally suppressing the body's immune system. Usually, infections can be diagnosed and treated, however more rarely they can be life threatening. 3. Stomach upset, dizziness, headaches, cold like symptoms (fever, chills, nausea, and vomiting), changes in blood pressure, sore joints, and skin rash. 4. Very rarely, a serious brain infection may occur (Progressive multifocal leukoencephalopathy PML).	When acutely unwell, this medication may be used to help speed up recovery. More rarely, this drug is used as a regular treatment for prevention of worsening. Only used to treat children under 16 if the risk to their health as a result of autoimmune encephalitis is very high.	Usually two infusions (once and again in two weeks), given 6-12 monthly depending on blood counts.
Cyclophosphamide	Side effects include: 1. Nausea, vomiting and diarrhoea. 2. Bone marrow suppression which may lead to infections (as many drugs above), but also higher doses are associated with cancers and infertility. These risks are related to the total dose administered. 3. Bladder irritation can occur, often with bleeding. This can lead to bladder cancer, but this risk is significantly reduced with co-administration of 'mesna' (adjuvant drug – modifies other ingredients enhances body's immune response). 4. Other side effects include vomiting, nausea, diarrhoea, hair loss, heart and lung toxicity, increased cancer risk, increased risk of bladder infections, ulcers,	This medication may be used to treat the acute episode by encouraging a gradual improvement and preventing relapses. Its effects can last several months. Avoided during pregnancy or if attempting a pregnancy.	Repeated intravenous treatments, usually cycles of 3-6 months.

	irregular periods, infertility, and potential to cause foetal abnormalities		

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Thank you!

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