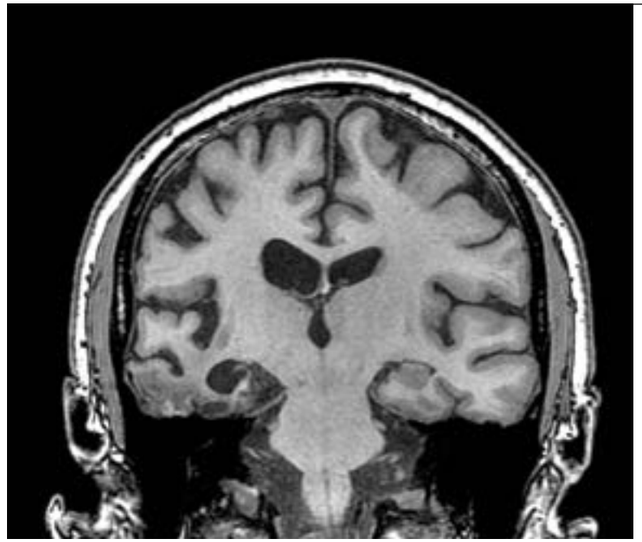

WHAT IS ENCEPHALITIS?

A nuts-and-bolts guide to the inflammatory brain condition, by **Dr Ava Easton**, the Chief Executive Officer of the Encephalitis Society.

Encephalitis is simply inflammation of the brain. It can be caused, in very broad terms, one of two ways: either through an infection (ordinary, everyday infections, such as the flu, herpes simplex and measles, among others) bareaching the blood-brain-barrier and mounting a direct infectious attack on the brain, or through a person's own immune system detecting something it considers unfamiliar (these might be tumours, or proteins in the brain), and the immune system attacking the brain in error.

Infectious and autoimmune encephalitides can, however, present in very different ways. Infectious encephalitis often has a very rapid onset, while autoimmune encephalitis can present over days, weeks and in some cases months. These, as we will go on to illustrate, can have important consequences for patients.

Global incidence figures are difficult to ascertain, due to variations, such as geographic distribution of causative agents, immunisation policies of different countries, and methodological issues, such as how cases are defined, diagnosed and recorded. It is estimated that there are around 500,000 cases a year worldwide: one person every minute. This is likely an underestimate. Add to this the fact that in many countries encephalitis has a higher incidence than motor neuron disease (MND or ALS), multiple sclerosis (MS) cerebral palsy, and bacterial meningitis, then it seems anomalous that despite these conditions being less

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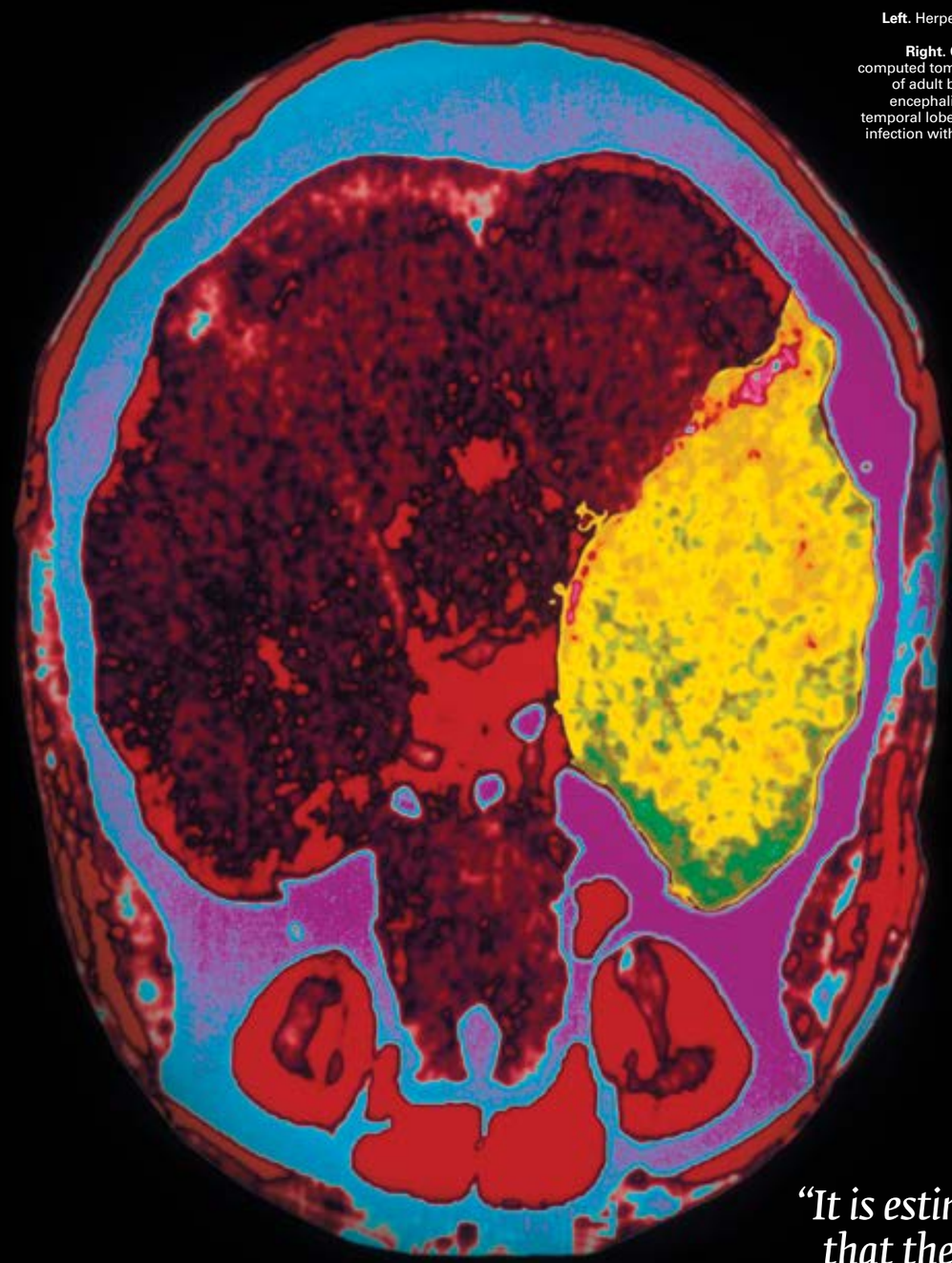


Left. Herpes encephalitis temporal lobe
Right. Coloured axial computed tomography scan of adult brain, showing encephalitis in the right temporal lobe caused by an infection with herpes virus.

KEY MESSAGES

- Encephalitis (inflammation of the brain) is a serious and often devastating neurological condition.
- Encephalitis can be caused by infection or by a person's own immune system.
- Brain imaging and lumbar puncture are critical to diagnoses.
- Patients can be left with an acquired brain injury and will need ongoing therapeutic treatment and support.
- The Encephalitis Society is a source of support and information for patients, families, those left bereaved and professionals involved with the condition.

"It is estimated that there are around 500,000 cases a year worldwide: one person every minute"

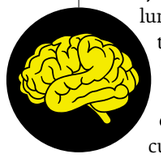
common, they receive a much higher clinical and public profile than encephalitis. Independent polling commissioned by the Encephalitis Society tells us that around the world still eight out of 10 people have not heard of the condition.

Mortality is higher than many other neurological diseases, and may be even more so in low- to middle-income countries, particularly where vaccination programmes do not exist for preventable forms of the condition, such as measles encephalitis and Japanese encephalitis.

Diagnosis and treatment

Diagnosis of encephalitis is often considered a diagnosis of exclusion. Patient history is important: pre-existing conditions that might affect immunity – for example, HIV; history of mental health, drug or alcohol abuse; or exposure to infections, such as measles, mumps or chickenpox. Also, have they travelled out of the country recently (could they have been bitten by ticks or mosquitoes that may have been carrying infection)? Or, through their occupation, could they have been exposed to toxins or chemicals?

Bloods will be taken for blood and serum testing and patients are usually tested for HIV. Brain imaging and lumbar puncture are perhaps the two most important elements in reaching an encephalitis diagnosis – looking for evidence of brain inflammation and of current or recent infection. Testing of serum is important because of autoimmune causes. In some cases, where diagnosis is proving difficult, a brain biopsy may be conducted.



Diagnostic and management guidelines for infectious causes exist for various countries and guidelines for autoimmune causes are in development.

Where infectious types of encephalitis are suspected, a drug called acyclovir is administered, often as a precaution (it is critical in the treatment of a herpes encephalitis). Antibiotics will be given if bacteria are suspected, however, viral causes are much more common. Fungal and parasitic causes are also a possibility, but rare. Other infectious causes generally have to run their course and are reliant on the patient's immune system.

Patients who have an autoimmune cause are treated with a range of immuno-modulatory therapies, such as high-dose steroids, immunoglobulin and plasma exchange. Autoimmune patients are at risk of relapsing disease and sometimes second-line therapies, such as rituximab and cyclophosphamide, are introduced as part of their treatment plan. Where there is an underlying cause, such as a tumour, it will need to be removed or treated to inhibit the immune system response.

Outside of this, treatment is symptomatic and typically involves standard nursing care: ventilation, monitoring of consciousness and respiration, sedation, anti-convulsants, and treatments to address secondary infections along with keeping the patient hydrated.

One particular element that complicates diagnosis and treatment is the two diverse ways that infectious and autoimmune encephalitides can present. In particular, autoimmune encephalitis can present as psychiatric in nature and these patients can go down psychiatric pathways, in some cases for weeks and months, before something occurs in their presentation, that may raise a neurological red flag. Understandably, this can have a significant impact on outcomes both physically and psychologically for patients.

Outcomes and quality of life

Whilst some people may make a good recovery, the long-term consequence of encephalitis for many is life-changing and results in an acquired brain injury. The consequences of which can be cognitive, physical, behavioural, emotional and psycho-social. People may experience changes in their view of themselves (or their relatives). This is both fuelled and exacerbated by memory problems, changes in personality, feeling different, and loss of emotions, thoughts or behaviour. Returns to work and education can result in repeated failure in some case and with this comes additional challenges with mental and emotional well-being.

The range of outcomes can be wide-ranging, and rates of recovery in survivors less than for some other forms of acquired brain injury. This latter point can be in response to a range of issues (such as challenges in understanding and making sense of a condition most people have never heard of; a lack of collective understanding in people's social circles and communities in relation to the outcomes of the condition; and as a result of being discharged often more quickly than other brain injury groups because encephalitis survivors rarely have the orthopaedic or physical injuries that accompany some other forms of brain injury) and has direct consequences for quality of life post-illness. Neuropsychology and neuropsychiatry are often critical interventions in the recovery of patients post-encephalitis. BMS

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ENCEPHALITIS SOCIETY

Although based in the UK, the reach of the Encephalitis Society is worldwide. The vision of the Encephalitis Society is a world aware of encephalitis, its consequences and the support available. Its mission is to increase global awareness of encephalitis, saving lives and building better futures, and it works to improve the quality of life of all people affected directly and indirectly by encephalitis, by providing support and information for patients, families and professionals, by raising awareness (its primary driver in this is World Encephalitis Day on 22 February each year), and by funding and collaborating on research into the condition. It's work is evidence-based, peer-reviewed, benefits from a world-renowned scientific panel and has won numerous awards, including two highly commended from the British Medical Association and Charity of the Year.

SYMPTOMS OF ENCEPHALITIS

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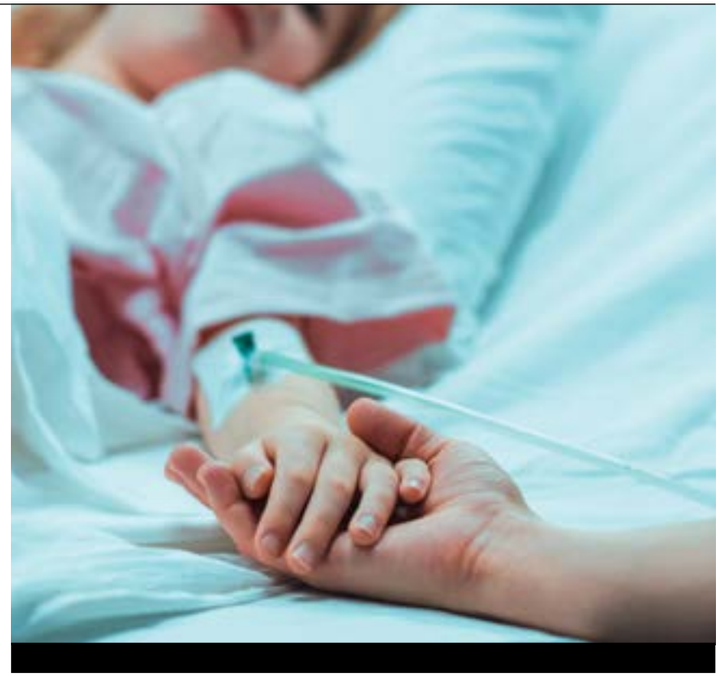
Infectious encephalitis	Autoimmune encephalitis
• Flu-like symptoms • Dizziness • Malaise • Headache • Vomiting/gastrointestinal upset • Fever. **Later stages indicating a more serious illness involve lowered consciousness which may include:** • Confusion/drowsiness/seizures/coma. **Other symptoms may include:** • Photo-sensitivity/sensory change/inability to speak or control movement • Uncharacteristic behaviour.	**Symptoms will vary depending on the particular autoimmune cause but may include:** • Confusion • Altered personality or behaviour • Psychosis • Movement disorders • Repetitive, involuntary motor or vocal tics • Seizures • Hallucinations • Memory loss • Sleep disturbance.



CASE STUDY: LIFE HAS CHANGED DRASTICALLY

Tricia describes Maddilyn's journey with an autoimmune encephalitis: anti-NMDA-receptor encephalitis.

Maddilyn was a typical five-year-old: silly, loud, full of energy, and a bit sassy. She had always been a kind and affectionate child. She was helpful and mindful of others, until one day she wasn't.

Suddenly, Maddilyn became sarcastic, aggressive, and combative. Everyday things became a struggle. Our bright, silly, carefree dreamer had morphed overnight into an angry, moody, sad child. Her father and I attributed her change in behaviour to the stressors in life: starting school, family illness and the addition of a new sibling. But when the behavioural interventions we normally used stopped working and her behaviour escalated into violence, while at the same time she refused to eat or sleep, we knew something more was wrong.

On 17 May, 2016 after months of aggressive behaviours, refusing to eat, endless sleepless nights, and no answers, she suffered a seizure and was given the diagnosis of anti-NMDA receptor antibody encephalitis.

A quick search of the internet left me feeling overwhelmed. I learned that NMDA is treatable and that outcomes are good with early diagnosis. It was unclear at what point in the disease Maddilyn was, but her titres were apparently excessively high. She was immediately started on IV steroids and intravenous immunoglobulin and within hours she was awake, smiling, and asking for food for the first time in two weeks.

She has had multiple drugs and therapies, and is better in many ways, but at the same time, not better at all. Since diagnosis, Maddilyn struggles with managing a variety of symptoms: headaches, fatigue, nausea, random pain and blurred vision, she struggles to formulate thoughts, remember things; she struggles with focusing attention and controlling impulses. She has mood swings, is often anxious, and is easily overwhelmed by stimulus.

Our life as a family has changed, drastically. Maddilyn has a central line that requires daily care. She no longer has independence to shower and requires help. She has weekly infusion appointments that sometimes take the whole day. She's hospitalised every other week for treatment. Medications changed her physical body. She has lost the innocence of childhood, because she has seen and been through far more than any child should. As her parents, we have lost the blind ignorance that allowed us to sleep at night. We live on the edge of anxiety and analyse every behaviour for signs of relapse. Raising awareness of the condition has been a huge part of Maddilyn's treatment and our healing.

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