Herpes simplex virus encephalitis (HSE)  
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What is herpes simplex virus encephalitis (HSE)?
HSE is a type of infectious encephalitis which happens when herpes simplex virus (HSV) enters the brain.

Usually people get infection of the mouth and throat with HSV1 early in life often without symptoms. The virus attaches to, and enters sensory nerves in the throat and moves to nerve cells called ‘ganglia’ (e.g. the trigeminal ganglia). Here the virus establishes a latent (hidden) and life-long infection. In some people, from time to time, the virus may reactivate to produce recognisable lesions such as cold sores around the lips and nose.

While HSV 1 is widespread, HSE is rare. How HSV gains access to the brain is not known, there are various hypotheses such as via the blood stream or via nerves but there is no definite evidence to support any of the suggested routes to date.

Whichever way HSV 1 gains access to the brain, in the acute illness, the damage that results from the viral infection and associated inflammation is often severe. Typically, the virus is initially present in a part of the brain called the limbic cortex. It may then spread to the adjacent frontal and temporal lobes of the brain. It is the destruction of tissue in these areas together with brain swelling from the inflammation, which causes many of the symptoms.

Symptoms of HSE
HSE usually develops over a period of days but, like any other viral infection, depending, for example, upon the immunity of the patient, the disease may take a variable course. Typically, it begins with ‘flu-like’ symptoms followed by neurological deterioration, which may include personality and behavioural changes, seizures, weakness and difficulties in communication. If untreated it may lead to progressive impairment of consciousness, coma and death.
Diagnosis
The rapid onset and development of HSE presents a dilemma to the clinician. During the early stages, when treatment would be most effective, the symptoms can be very general, so there may be several possible diagnoses.

Brain imaging by computerised tomography (CT) scan, or, for a clearer picture, a magnetic resonance imaging (MRI) is helpful. Sometimes an electro-encephalogram (EEG) to monitor the brain’s electrical activity assists diagnosis. These procedures, together with careful and continuous clinical assessment, provide data which may be suggestive of HSE but, also importantly, may exclude other conditions.

The key diagnostic procedure is a lumbar puncture (LP) to take some of the fluid bathing the brain and spinal cord (cerebrospinal fluid CSF) for laboratory analysis. One of the tests called the polymerase chain reaction (PCR) is very sensitive at detecting low levels of viruses’ genetic fingerprints. In general, the test is useful for up to 10 to 20 days after the onset of neurological disease and then usually becomes negative. At this time, a further procedure for the detection of herpes virus antibody in the CSF can be used. This also provides an accurate diagnosis. This latter test is often used as a follow up to the initial PCR test(s). When a patient is admitted to hospital, because of the 'vague' nature of the symptoms (in some cases) a lumbar puncture may not be performed immediately. This is unfortunate because the LP is an accurate test, which provides a diagnosis at the time when treatment is most helpful to the patient. However, a PCR test should always be carried out as soon as possible in all suspected cases of HSE.

Treatment
If therapy with a drug called Aciclovir (which reduces replication of the virus) can be started during the first few days of the illness (48 hours), there is a dramatic reduction in the mortality rate from around 70-80% down to 10-20%. The provision of high levels of nursing care and the management of complications such as brain oedema (i.e. swelling) are also key factors, which influence the outcome of HSE.

National UK guidelines recommend a minimum 14-day course of treatment with Aciclovir into the veins in adults. Towards the end of this period, the LP should be repeated and PCR analysis of the CSF performed. If the PCR no longer detects HSV the treatment can be stopped; if HSV is identified, the treatment should continue with repeat lumbar punctures at 7-
day intervals until the absence of HSV is confirmed. More information on these guidelines can be found in *Management of Suspected Viral Encephalitis in Adults and Children*, publication found on our website or requested from our office.

**Outcomes and prognosis**

The reduction in HSE mortality has led to a paradoxical situation. There are without doubt more survivors, but many may suffer from permanent neurological and/or psychological deficits, for example amnesia (memory loss). Improvements are still needed to both speed diagnosis and improve treatment.

Recent research has identified that HSE may sometimes be followed by a rare complication: development of a second encephalitis. This encephalitis is autoimmune and characterised by the presence of antibodies in the patient's blood against a brain protein—the NMDA receptor. The anti-NMDA receptor encephalitis is treated differently to HSE. For more information on this type of autoimmune encephalitis please see the Anti-NMDA receptor encephalitis and Immunotherapy in autoimmune encephalitis factsheets.

The message is that our understanding of conditions such as viral encephalitis is continually developing. However, these are complex conditions and whilst it is unlikely that encephalitis will be preventable (in the near future) the prospect for the rapid and efficient diagnosis for many of these conditions will improve during coming years. The consequence of improved and rapid diagnosis is that early treatment—which is so important—can and will increasingly be introduced.

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