Encephalitis: Time Is Brain, Too

Updated to EAN–ESCMID 2026 · infectious and autoimmune, from the first hour to recovery

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PRE-TEST · QUESTION 1 OF 3

The negative PCR

A 58-year-old has two days of fever and confusion. CSF: 80 lymphocytes. MRI: left mesial temporal FLAIR signal. Aciclovir was started. HSV PCR on CSF taken 36 hours into the illness is negative.

A Stop aciclovir: the PCR is negative

B Continue aciclovir and repeat the lumbar puncture in 2–3 days

C Switch to oral valaciclovir and discharge

D Add dexamethasone, and stop aciclovir if he improves

The psychiatric ward

A 22-year-old woman has ten days of new psychosis. She now has orofacial dyskinesias, one generalised seizure and swings of heart rate. MRI brain is normal. Which test is most useful now?

A Serum thyroid peroxidase antibodies

B CSF NMDA receptor antibodies, with pelvic imaging

C Repeat MRI in one month

D Urine toxicology only

PRE-TEST · QUESTION 3 OF 3

The steroid question

HSV-1 encephalitis is confirmed and aciclovir is running. A colleague asks whether adding dexamethasone will improve the patient's memory outcome.

A Yes: the benefit is proven, give it routinely

B No: steroids are harmful with active viral replication

C No proven benefit; guidelines advise neither for nor against, and it appears safe

D Only if the HSV PCR is negative

Where we are going

1 **A short history**
From Babylon to Vienna to the antibody era

2 **Foundations**
What counts as encephalitis, and what causes it

3 **The first hours**
Recognise, puncture, treat, image

4 **Infectious**
Herpes simplex first, then geography

5 **Autoimmune**
NMDA receptor, limbic, brainstem, mimics

6 **ICU and recovery**
Seizures, pressure, prognosis, rehabilitation

7 **Take home**
Ten rules and the pre-test answers

PART 1

A short history

Every rule we follow at the bedside was paid for by an epidemic, a trial or a single patient.

A SHORT HISTORY

Babylon, 323 BC

Alexander the Great and West Nile Virus Encephalitis

John S Marr [*], Charles H Calisher [†,✉]

▸ Author information

▸ Copyright and License information

PMCID: PMC3034319 PMID: 14725285

Marr JS, Calisher CH. Emerg Infect Dis 2003;9:1599–1603.

Alexander the Great dies at 32 after two weeks of fever, weakness and delirium.

Plutarch notes that ravens fell dead at the city gates as he arrived.

Dead birds, then a febrile encephalitis with flaccid weakness: two epidemiologists read that as West Nile virus.

Unprovable. But the question stands: what were the animals doing?

Before it had a name

1529	**The English sweats**	England
1597	**Mal mazzuco**	Italy
1672–75	**Kriebelkrankheit**	Germany
1754–57	**Rafania**	Sweden
1890–91	**Nona**	Italy

Epidemics of fever, stupor and abnormal movements that Crookshank, writing in 1918, thought were the same disease returning.

Crookshank FG. A note on the history of epidemic encephalomyelitis. Proc R Soc Med 1919;12:1–21.

Vienna, 1917: the sleeping sickness



An emergency ward during the 1918 influenza pandemic, which overlapped with encephalitis lethargica.

- Constantin von Economo describes encephalitis lethargica
- A decade-long pandemic; estimates reach a million cases
- It disappears by the late 1920s
- Survivors develop parkinsonism years later
- 1969: Oliver Sacks, levodopa and Awakenings

The cause is still unknown.

Japan: a summer disease

1871	First clinical case recorded in Japan
1924	Epidemic of more than 6,000 cases
1930s	Virus isolated from human brain
1950s	Mosquito, pig and bird cycle understood; vaccine

Still about 100,000 cases a year, almost all preventable.

World Health Organization. Japanese encephalitis fact sheet.

A SHORT HISTORY

From a boy in Paris to aciclovir

1885 Pasteur vaccinates Joseph Meister, aged 9, after a rabid dog bite. He survives.

1941 Herpes simplex virus is isolated from the brain of a fatal case.

1977 Vidarabine: the first drug to cut mortality, from about 70% to 28%.

1986 Aciclovir beats vidarabine: mortality 28% against 54%.

1990s PCR on CSF replaces brain biopsy.

Whitley RJ, et al. N Engl J Med 1977;297:289–294. Whitley RJ, et al. N Engl J Med 1986;314:144–149.

2007: the brain on fire

2005 Dalmau: four young women with psychosis, coma and an ovarian teratoma.

2007 The target is found: the NMDA receptor.

2009 A 24-year-old reporter, thought to be psychotic, is asked to draw a clock. All twelve numbers go on one side.

2016 Graus criteria: we may treat before the antibody returns.

A bedside test, a clock and a pencil, changed the diagnosis.

Dalmau J, et al. Ann Neurol 2007;61:25–36. Cahalan S. Brain on Fire. 2012.

A SHORT HISTORY

A century in one line

1917	1924	1941	1986	1990s	2007	2016	2026
Encephalitis lethargica	**Japanese encephalitis**	**HSV isolated**	**Aciclovir**	**CSF PCR**	**NMDA receptor**	**Graus criteria**	**EAN–ESCMID, DexEnceph**
von Economo describes the epidemic	Epidemic of more than 6,000 cases	From the brain of a fatal case	Mortality 28% versus 54% on vidarabine	Brain biopsy is no longer needed	Dalmau: antibody and teratoma	Autoimmune encephalitis defined clinically	New guideline; steroid trial reports

Whitley RJ, et al. N Engl J Med 1986;314:144–149. Dalmau J, et al. Ann Neurol 2007;61:25–36. Graus F, et al. Lancet Neurol 2016;15:391–404.

PART 2

Foundations

What the word means, how we define a case, and what the causes are.

Three words that get confused

Encephalitis

Inflammation of the brain itself, with neurological dysfunction.

Proof: CSF, imaging or EEG.

Encephalopathy

Altered mental status from any cause: metabolic, toxic, septic, hypoxic. No inflammation required.

Meningitis

Inflammation of the meninges: headache, neck stiffness. Mental state preserved early.

Every encephalitis is an encephalopathy. Most encephalopathies are not.

The case definition

MAJOR · REQUIRED

Altered mental status for 24 hours or more

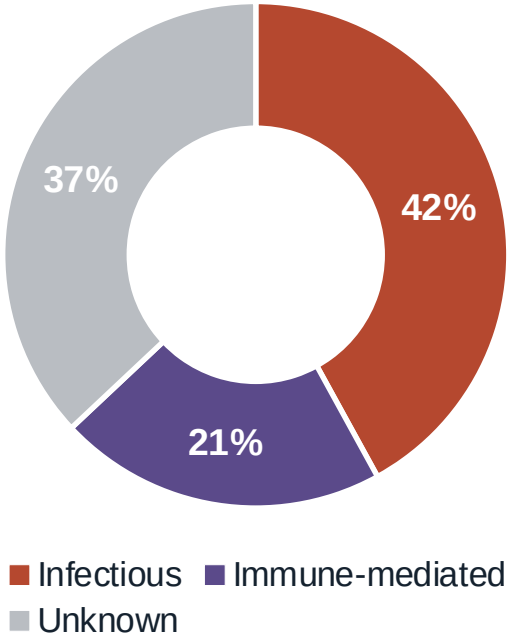
Reduced or altered consciousness, lethargy or personality change, with no other cause found.

MINOR · 2 = POSSIBLE · 3 OR MORE = PROBABLE

1. Fever of 38 °C or more within 72 hours
2. Seizures not explained by known epilepsy
3. New focal neurological signs
4. CSF white cells of 5 per mm³ or more
5. New parenchymal abnormality on imaging
6. EEG consistent with encephalitis

Venkatesan A, et al. Clin Infect Dis 2013;57:1114–1128.

What causes it



Infectious · 42%

HSV 19%, VZV 5%, M. tuberculosis 5%, then many rare agents.

Immune-mediated · 21%

ADEM 11%, NMDA receptor 4%, VGKC-complex 3%.

Unknown · 37%

Despite extensive testing. Many are probably autoimmune.

Granerod J, et al. Lancet Infect Dis 2010;10:835–844 (n = 203, England).

PART 3

The first hours

Recognise it, puncture early, start aciclovir within six hours, image within a day.

When to think of it

Fever, and a brain that is not working

- Confusion, drowsiness or coma
- New behaviour or personality change
- Seizures, often focal
- Aphasia, hemiparesis, cranial nerve signs
- Headache, with or without neck stiffness

No fever does not exclude it

Elderly, immunocompromised and autoimmune cases are often afebrile.

Ask the family

They report the personality change that the examination misses.

Ask where, when and what

Travel, season, mosquito or tick bites, animals, rash, vaccines, HIV status.

The first six hours

0 MIN

Suspect

Airway, glucose, seizures. Blood cultures, HIV test.

EARLY

Lumbar puncture

Do not wait for imaging unless there are signs of brain shift.

WITHIN 6 H

IV aciclovir

10 mg/kg every 8 hours. Never delayed for tests.

WITHIN 24 H

MRI brain

With diffusion and FLAIR. CT only to make the puncture safe.

SELECTIVE

EEG

Suspected seizures, or psychiatric versus organic.

Add antibiotics whenever bacterial meningitis is possible.

Granerod J, et al. EAN–ESCMID guideline. Eur J Neurol 2026. Tunkel AR, et al. Clin Infect Dis 2008;47:303–327.

Lumbar puncture: image first if

CT BEFORE THE NEEDLE WHEN THERE IS

- GCS below 13, or a fall of more than 2
- Focal neurological signs, including unequal or poorly reactive pupils
- Papilloedema
- Abnormal posture or doll's eye movements
- Seizures until stabilised
- Relative bradycardia with hypertension
- Immunocompromise

DELAY IT, WHATEVER THE SCAN SHOWS, FOR

- Shock or respiratory compromise
- Suspected meningococcal septicaemia
- Infection at the puncture site
- Coagulopathy or anticoagulation: next two slides
- CT: brain shift or tight basal cisterns

SEND THE CSF FOR

Opening pressure, cells, protein, paired glucose, lactate, Gram stain and culture. PCR for HSV-1, HSV-2, VZV and enterovirus. Store a sample.

If the needle waits, aciclovir does not. Look again at 12 hours.

Solomon T, et al. J Infect 2012;64:347–373. McGill F, et al. J Infect 2016;72:405–438.

Lumbar puncture: the numbers

≥ 40

Platelets, $\times 10^9$/L. Between 20 and 40: decide case by case with haematology. A rapidly falling count is a reason to wait.

≤ 1.4

INR on warfarin, checked on the day. Urgent: vitamin K 5 mg IV works in 6–8 hours; add prothrombin complex if sooner.

≤ 1.4

APTT ratio on intravenous heparin, with the infusion stopped 4–6 hours before.

TWO THINGS THAT CHANGED

- The 2012 encephalitis guideline said platelets below 100. Guidance written for the question since then uses 40.
- Routine clotting tests are not needed before every puncture. Wait for them only when the history, examination or drug chart suggests a bleeding tendency.

Dodd KC, et al. ABN guideline. Pract Neurol 2018;18:436–446. McGill F, et al. J Infect 2016;72:405–438.

Lumbar puncture on antithrombotics

Drug	Last dose before	Restart after	If it cannot wait
Aspirin	No need to stop	Continue	Proceed
Clopidogrel, prasugrel, ticagrelor	7 days	6 hours	Consent; discuss platelets
LMWH, prophylactic dose	12 hours	4 hours	Wait 12 hours
LMWH, treatment dose	24 hours	4 h; 24 h if traumatic	Wait 24 hours
Heparin infusion	4–6 hours, APTT ratio ≤ 1.4	1 hour	Stop, recheck APTT
Warfarin	5 days, INR ≤ 1.4	12 hours	Vitamin K, then PCC
Apixaban, rivaroxaban	At least 24 hours	6 hours	Haematology advice
Dabigatran	At least 48 hours	6 hours	Idarucizumab

Dodd KC, et al. ABN guideline. Pract Neurol 2018;18:436–446. Elective intervals; DOACs assume CrCl ≥ 50 mL/min. PCC: prothrombin complex.

Reading the CSF

	Cells per mm³	Protein	Glucose	Remember
Viral	5–500, lymphocytes	Mildly raised	Normal	Can be normal early in HSV
Bacterial	100s–1000s, neutrophils	High	Low	Listeria may be lymphocytic
Tuberculous, fungal	10s–100s, lymphocytes	High	Low	Subacute; basal meningitis
Autoimmune	Normal or under 100	Normal or mild	Normal	Oligoclonal bands; antibody in CSF

Tunkel AR, et al. Clin Infect Dis 2008;47:303–327. Graus F, et al. Lancet Neurol 2016;15:391–404.

Three PCR traps

1

Too early

HSV PCR can be negative in the first 72 hours. If suspicion remains, repeat the lumbar puncture after 2–3 days.

2

The wrong test

Multiplex panels had a pooled sensitivity of about 76% for HSV-1. Do not let them replace pathogen-specific PCR.

3

One result

Stop empirical aciclovir only when the PCR is negative and the clinical picture, CSF and imaging do not fit HSV.

Granerod J, et al. EAN–ESCMID guideline. Eur J Neurol 2026;doi:10.1111/ene.70647.

MRI: where is the signal

Mesial temporal and insula

Asymmetric; basal ganglia spared

Herpes simplex

Thalami and basal ganglia

Bilateral

Japanese, West Nile

Brainstem and cerebellum

Rhombencephalitis

Enterovirus A71, Listeria

Both mesial temporal lobes

Symmetric, no diffusion restriction

Limbic: LGI1, GABA-B

Normal

In about two thirds

NMDA receptor encephalitis

Multifocal white matter

Large, poorly defined lesions

ADEM, MOG antibody disease

Titulaer MJ, et al. Lancet Neurol 2013;12:157–165. Graus F, et al. Lancet Neurol 2016;15:391–404.

EEG: when it earns its place

Order it when

Seizures are suspected, the patient is not waking, or a psychiatric picture might be organic.

Herpes simplex

Temporal slowing; lateralised periodic discharges over the affected temporal lobe.

What a normal EEG tells you

A normal awake background makes encephalitis unlikely. Diffuse slowing is common and non-specific.

NMDA receptor

Extreme delta brush in about 30% of adults on continuous EEG; it marks a longer illness.

Granerod J, et al. Eur J Neurol 2026. Schmitt SE, et al. Neurology 2012;79:1094–1100. Practise the patterns free at learneeg.thetract.org

PART 4

Infectious encephalitis

Herpes simplex first, because it is common, lethal and treatable. Then the causes that depend on where you practise.

Herpes simplex: do not miss it

~90%

of adult cases are HSV-1; HSV-2 in neonates and in meningitis

~70%

mortality without treatment

96–98%

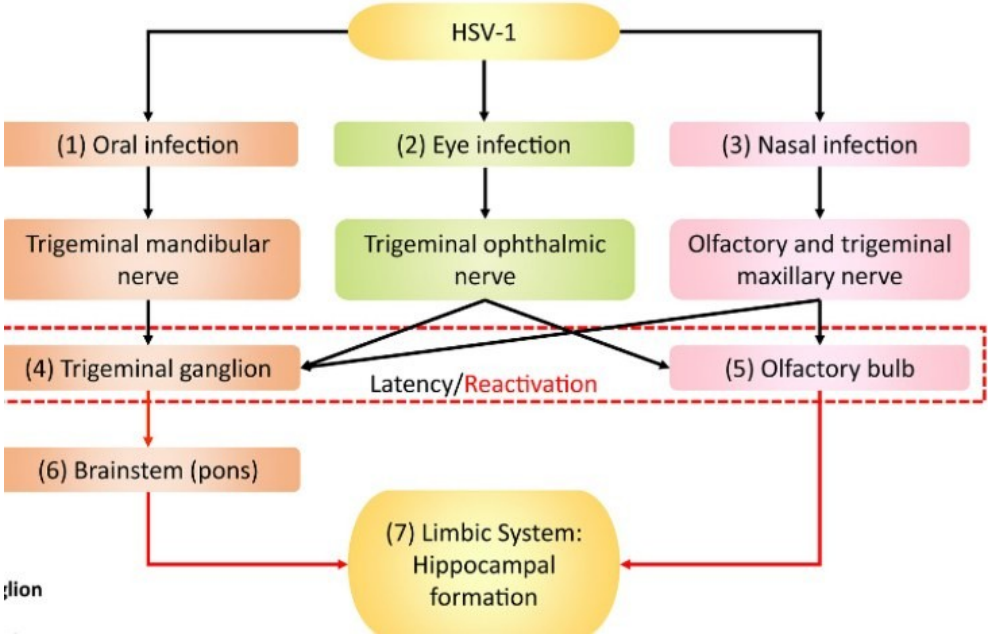
sensitivity of CSF PCR after the first days

WHY THE TEMPORAL LOBE

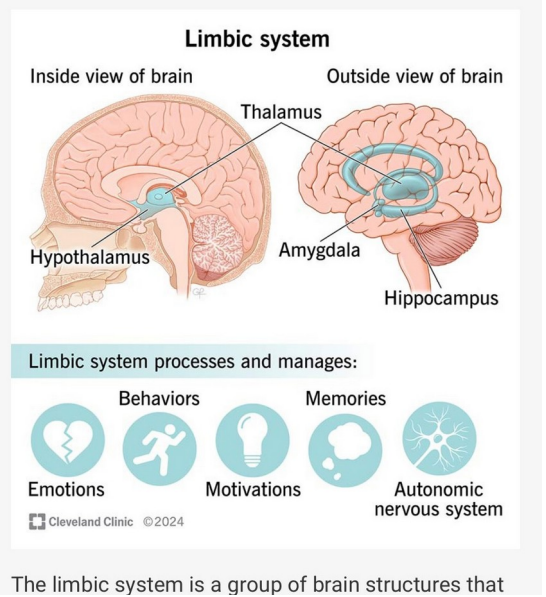
The virus travels the olfactory and trigeminal pathways to the mesial temporal and orbitofrontal cortex. So the illness speaks in limbic terms: memory, behaviour, smell, language, and temporal lobe seizures.

Tunkel AR, et al. Clin Infect Dis 2008;47:303–327. Whitley RJ, et al. N Engl J Med 1986;314:144–149.

The route into the brain



Routes of HSV-1 from the periphery to the limbic system, with latency in the trigeminal ganglion and olfactory bulb.



The limbic system. Illustration: Cleveland Clinic.

How it presents, what tests show

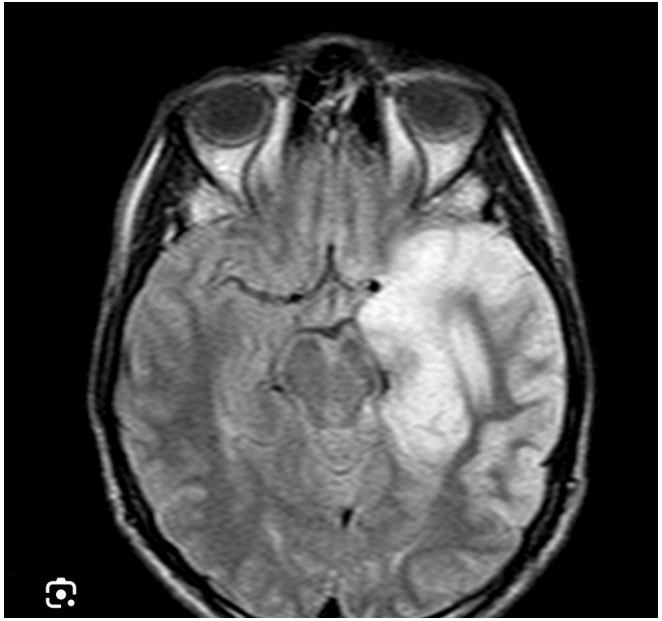
AT THE BEDSIDE

- Fever and headache over days
- Personality change, odd behaviour
- Aphasia, memory loss
- Focal seizures; olfactory aura
- Drowsiness progressing to coma

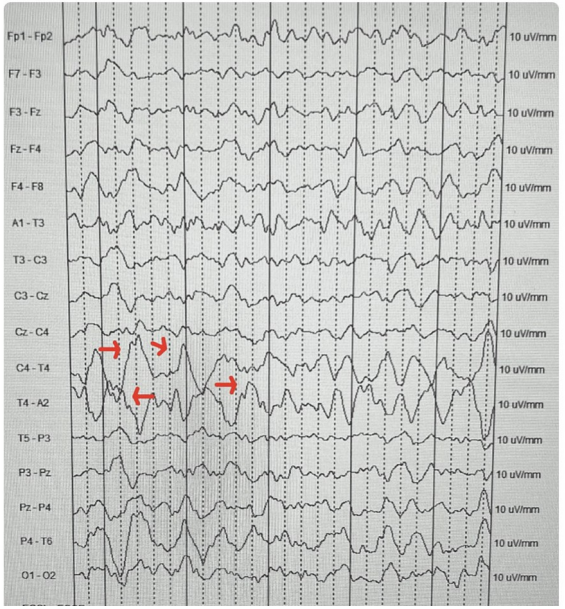
CSF	Lymphocytes, raised protein, normal glucose. Normal in a minority at first.
MRI	Asymmetric mesial temporal, insular and cingulate signal, restricted diffusion early.
EEG	Temporal slowing or lateralised periodic discharges.
PCR	HSV DNA in CSF. Repeat at 2–3 days if negative and still suspected.

Solomon T, et al. J Infect 2012;64:347–373. Granerod J, et al. Eur J Neurol 2026.

What it looks like



FLAIR MRI: left temporal and insular hyperintensity with swelling, basal ganglia spared.



EEG at presentation with focal temporal spikes (arrows), from a published case report.

Aciclovir, done properly

10 mg/kg

intravenously every 8 hours

At least 14 days.
21–28 days if severe, slow to improve or immunocompromised.

The delay is the danger

Starting more than 2 days after admission predicted a poor outcome.

Protect the kidney

Hydrate, infuse over an hour, dose for renal function. Watch for crystal nephropathy.

No oral tail

Three months of valaciclovir after IV treatment did not improve outcome.

Granerod J, et al. Eur J Neurol 2026. Raschilas F, et al. Clin Infect Dis 2002;35:254–260. Gnann JW, et al. Clin Infect Dis 2015;61:683–691.

Steroids in HSV: the 2026 answer

DEXENCEPH · LANCET NEUROLOGY 2026

94 adults, 53 hospitals

Aciclovir with or without dexamethasone.

Verbal memory at 26 weeks: no significant difference.

No safety signal.

Guideline position

No recommendation for or against steroids in confirmed HSV encephalitis.

If already given

Empirical steroids for another suspected cause are unlikely to be harmful.

What it means

Not routine for memory. Not feared when oedema demands.

Solomon T, et al. DexEnceph. Lancet Neurol 2026 (published 21 January 2026). Granerod J, et al. Eur J Neurol 2026.

Closer to home: Abha

Insights into adjunctive corticosteroid therapy in fulminant herpes simplex virus encephalitis: case analysis with contrasting outcomes

Hussein Algahtani[1], Bader Shirah[2], Hussam A. Jamaluddin [1], Nawal Abdelghaffar[1,3]

[1]Neurology Section, Department of Medicine, Aseer Central Hospital, Abha, Saudi Arabia

[2]Department of Neuroscience, King Faisal Specialist Hospital & Research Centre, Jeddah, Saudi Arabia

[3]Department of Neurology, Kasr Al Ainy Hospital, Faculty of Medicine, Cairo University, Cairo, Egypt

Algahtani H, et al. Case analysis from Aseer Central Hospital, Abha.

Fulminant HSV encephalitis treated with adjunctive steroids: contrasting outcomes from one patient to the next.

The trial later said the same at scale: no consistent benefit, and a decision made patient by patient when swelling threatens.

The relapse that is not viral

27%

developed autoimmune encephalitis after HSV encephalitis (14 of 51)

~1 month

median time to onset; nearly all within 3 months

WHEN A RECOVERING PATIENT WORSENS

- Repeat the lumbar puncture: HSV PCR is usually negative
- Send NMDA receptor and other neuronal antibodies in CSF and serum
- Adults: psychiatric and cognitive change. Children: choreoathetosis
- Treat as autoimmune encephalitis; restart aciclovir until PCR is back

Armangue T, et al. Lancet Neurol 2018;17:760–772. Granerod J, et al. Eur J Neurol 2026.

Beyond herpes simplex

Virus	The clue	Treatment
Varicella zoster	Rash may be absent; vasculopathy with infarcts	IV aciclovir 10–15 mg/kg 8-hourly
Enteroviruses	Children, summer; A71 hits the brainstem	Supportive
Japanese encephalitis	Rural Asia; thalamic signal, parkinsonism	Supportive; vaccine prevents
West Nile	Mosquito season; tremor, flaccid paralysis	Supportive
Rabies	Animal bite; hydrophobia, agitation, or paralysis	Prophylaxis after exposure only
CMV, HHV-6, JC	Advanced HIV, transplant recipients	Ganciclovir or foscarnet

Tunkel AR, et al. Clin Infect Dis 2008;47:303–327. WHO fact sheets: Japanese encephalitis; rabies.

Geography is a diagnostic test

South and East Asia

Japanese encephalitis, Nipah, scrub typhus, dengue

Europe, North Asia

Tick-borne encephalitis, West Nile, Toscana virus

The Americas

West Nile, St Louis, equine encephalitides, Powassan

Africa

Cerebral malaria, rabies, trypanosomiasis, HIV-related

Arabian Peninsula

Rift Valley fever, dengue, brucellosis, tuberculosis, rabies

Everywhere

HSV, VZV, enteroviruses, and autoimmune disease

Tunkel AR, et al. Clin Infect Dis 2008;47:303–327. WHO Disease Outbreak News: Rift Valley fever, Saudi Arabia and Yemen, 2000.

Not a virus, and needs another drug

Listeria

Over 50, pregnant or immunocompromised; brainstem signs

Ampicillin, not a cephalosporin

Tuberculosis

Weeks, not days; low glucose; basal enhancement, hydrocephalus

Four drugs and dexamethasone

Rickettsia

Rash, tick or mite exposure, low platelets

Doxycycline, early

Cerebral malaria

Travel or residence in an endemic area; any fever with coma

Blood film; IV artesunate

With advanced HIV

Cryptococcus: high opening pressure. Toxoplasma: ring lesions

Antigen tests; specific therapy

Neurosyphilis, brucella

Subacute; protean; ask about exposure

Serology in blood and CSF

Tunkel AR, et al. Clin Infect Dis 2008;47:303–327.

PART 5

Autoimmune encephalitis

As common as the infectious kind in the young, treatable, and diagnosed at the bedside before the antibody comes back.

Possible autoimmune encephalitis

1

Subacute onset

Under 3 months of working memory loss, altered mental status or psychiatric symptoms

2

At least one of

New focal CNS signs · new seizures · CSF pleocytosis · MRI suggestive of encephalitis

3

Others excluded

Infection, metabolic and toxic causes, tumour, and the mimics that follow

All three, then treat. The antibody confirms the diagnosis later; it does not make it.

Graus F, et al. A clinical approach to diagnosis of autoimmune encephalitis. Lancet Neurol 2016;15:391–404.

The antibodies worth knowing

Antibody	Typical patient	The clue	Tumour
NMDA receptor	Young women	Psychosis, dyskinesias, hypoventilation	Ovarian teratoma
LGI1	Men around 60	Faciobrachial dystonic seizures; low sodium	Rare
CASPR2	Older men	Neuromyotonia, insomnia: Morvan syndrome	Thymoma in some
GABA-B receptor	Adults, smokers	Limbic encephalitis with severe seizures	Small cell lung
Hu, Ma2, CRMP5	Older adults	Intracellular target; responds poorly	Lung, testis, thymus
GAD65 (high titre)	Women	Temporal lobe epilepsy, stiff person	Uncommon

Dalmau J, Graus F. Antibody-mediated encephalitis. N Engl J Med 2018;378:840–851.

AUTOIMMUNE

NMDA receptor: an illness in stages

DAYS	WEEK 1–2	WEEK 2–3	WEEK 3+	MONTHS
1	2	3	4	5
Prodrome	**Psychiatric**	**Neurological**	**Critical**	**Recovery**
Headache, fever, viral-like illness	Psychosis, agitation, insomnia, mutism	Seizures, orofacial dyskinesias, catatonia	Autonomic instability, hypoventilation, coma	In reverse order; cognition and behaviour last

Test the CSF: it is more sensitive than serum. Then look for the teratoma.

Dalmau J, et al. Lancet Neurol 2011;10:63–74. Gresa-Arribas N, et al. Lancet Neurol 2014;13:167–177.

NMDA receptor: what the cohort showed

577

patients; median age 21, four in five female

81%

good outcome at 24 months

53%

improved within 4 weeks of first-line therapy

12%

relapsed within 2 years

WHAT PREDICTED A GOOD OUTCOME

Early treatment, and no need for intensive care. In those who failed first-line therapy, second-line immunotherapy improved outcome. Patience is part of the treatment: recovery continues for 18 months or more.

Titulaer MJ, et al. Lancet Neurol 2013;12:157–165.

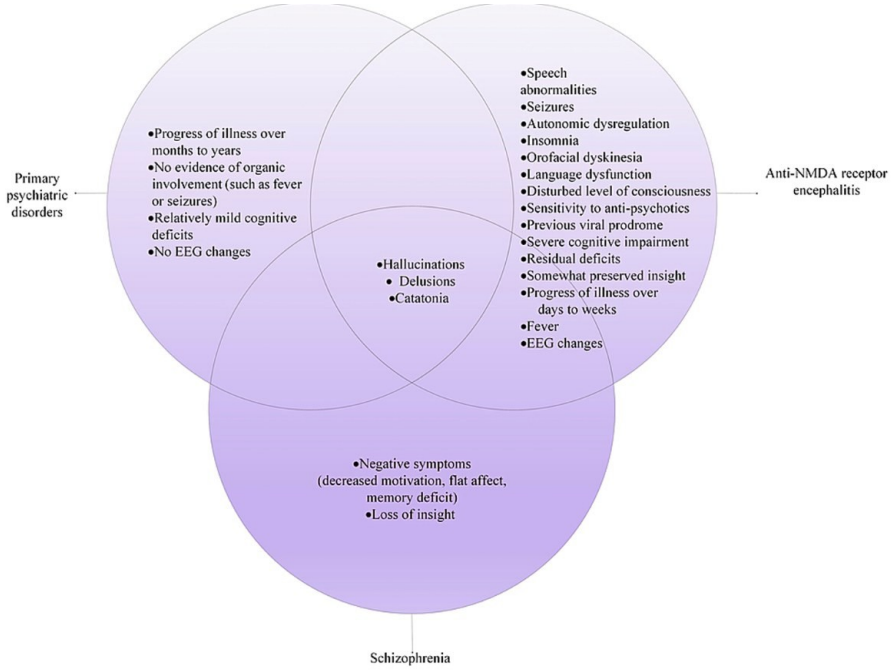
Psychiatry, or encephalitis

RED FLAGS IN A FIRST PSYCHIATRIC EPISODE

- Rapid onset, under 3 months
- Seizures
- Movement disorder or catatonia
- Autonomic disturbance
- Fluctuating consciousness
- Speech reduced or mute
- Severe reaction to antipsychotics
- Hyponatraemia
- Focal neurological signs
- Headache or a recent viral illness
- Known tumour
- Other autoimmune disease

Pollak TA, et al. Autoimmune psychosis: an international consensus. Lancet Psychiatry 2020;7:93–108.

Where the two overlap



Overlap of primary psychiatric disorders, schizophrenia and anti-NMDA receptor encephalitis.

Treatment is a ladder

Refractory

Tocilizumab, bortezomib; trials of newer agents are under way

Second line · no response at about 2 weeks

Rituximab, cyclophosphamide, or both

First line · start at once

IV methylprednisolone 1 g daily for 3–5 days, with IVIG 2 g/kg over 2–5 days or plasma exchange

Find the tumour

Pelvic ultrasound or MRI, CT chest, testicular ultrasound, by antibody and age.

Do not wait

Treat on the clinical criteria. Antibody results take days to weeks.

Abboud H, et al. Autoimmune encephalitis: best practice recommendations. J Neurol Neurosurg Psychiatry 2021;92:757–768.

AUTOIMMUNE

Bickerstaff brainstem encephalitis

1

Ophthalmoplegia

External, usually symmetrical

2

Ataxia

Gait and limb

3

Impaired consciousness

or hyperreflexia: the central sign

66%

anti-GQ1b IgG positive

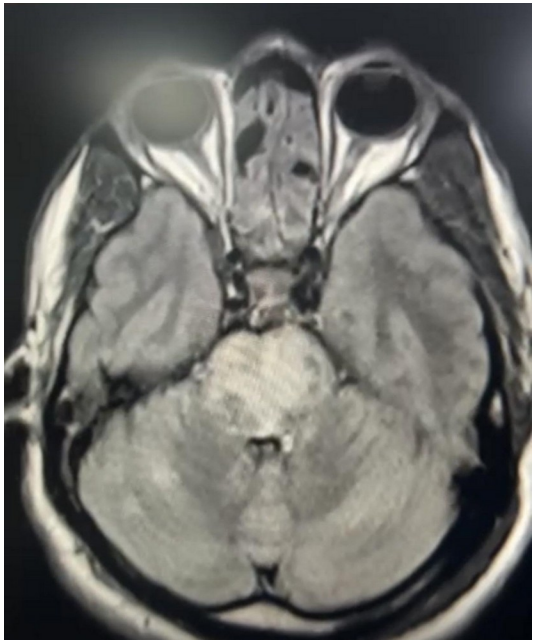
~30%

abnormal brain MRI

One spectrum: Miller Fisher syndrome (areflexia, alert), Bickerstaff (drowsy, brisk reflexes), and overlap with Guillain-Barré. Usually follows an infection.

Odaka M, et al. Bickerstaff's brainstem encephalitis: clinical features of 62 cases. Brain 2003;126:2279–2290.

A real case: coma and a bright pons



FLAIR: pontine hyperintensity

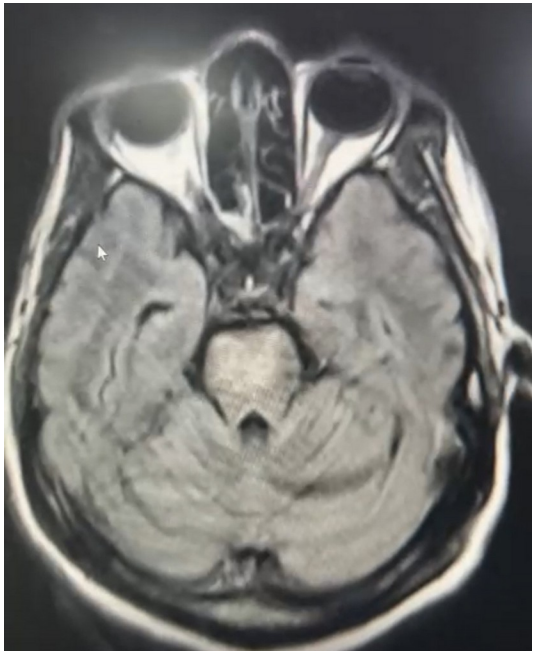
PRESENTATION

A 41-year-old man: vertigo, vomiting, then reduced consciousness and seizures. Intubated, GCS 3.

FIRST RESULTS

- CT and CT angiography: unremarkable
- CSF: high opening pressure, otherwise unremarkable
- MRI: pons, and two small right cerebellar lesions

The case: what happened next



COURSE

Five days of IVIG. Marked improvement, with regression on MRI. GCS 12 on a tracheostomy mask.

ALSO CONSIDERED

- Brainstem stroke
- Listeria rhombencephalitis
- MOG or aquaporin-4 disease

THE LESSON

A brainstem syndrome with a clean angiogram deserves an immune and infectious work-up.

The opposite error: over-diagnosis

107

adults misdiagnosed with autoimmune encephalitis

72%

did not meet criteria for possible autoimmune encephalitis

WHAT THEY REALLY HAD

- Functional neurological disorder
- Neurodegenerative disease
- Primary psychiatric illness
- Cognitive effects of comorbidity
- Tumour

THE TRAPS

- TPO antibodies: common in healthy people
- Low-titre GAD65
- VGKC without LGI1 or CASPR2
- Serum-only positives; an insidious course

Flanagan EP, et al. Autoimmune encephalitis misdiagnosis in adults. JAMA Neurol 2023;80:30–39.

PART 6

ICU and recovery

What kills in the first week, what limits life afterwards, and what prevents the disease.

Six problems in the ICU

1 Seizures

Often non-convulsive: continuous EEG if not waking

2 Raised pressure

Temporal swelling; osmotherapy, rarely decompression

3 Breathing

Central hypoventilation in NMDA receptor disease

4 Autonomic storms

Tachy- and bradycardia, pauses; monitor

5 Sodium

SIADH; hyponatraemia with LGI1

6 Fever and kidney

Control temperature; hydrate for aciclovir

Venkatesan A, Geocadin RG. Diagnosis and management of acute encephalitis: a practical approach. Neurol Clin Pract 2014;4:206–215.

Prognosis, and life afterwards

WHAT PREDICTS OUTCOME

- Delay to aciclovir or immunotherapy
- Age, and level of consciousness at the start
- Need for intensive care
- Extent of injury on MRI

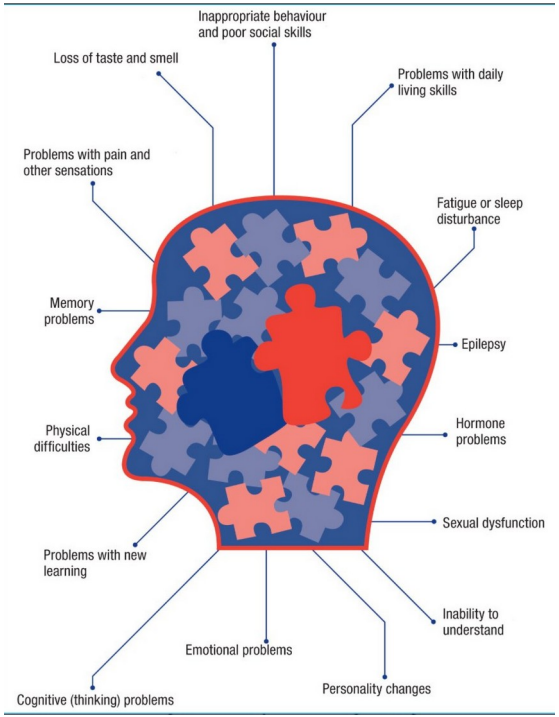
Only the first is in our hands.

PLAN BEFORE DISCHARGE

- Neuropsychological assessment: memory, behaviour
- Rehabilitation: cognitive, speech, occupational
- Epilepsy follow-up; driving and work advice
- Tumour surveillance after autoimmune disease
- Family support and patient organisations

Raschilas F, et al. Clin Infect Dis 2002;35:254–260. Titulaer MJ, et al. Lancet Neurol 2013;12:157–165. Solomon T, et al. J Infect 2012;64:347–373.

What survivors live with



- Memory and new learning
- Fatigue and disturbed sleep
- Personality and behaviour change
- Epilepsy
- Emotional problems, loss of confidence
- Loss of taste and smell

Tell the family before discharge, not at the first clinic visit.

Prevention is still the best treatment

~100,000

clinical cases of Japanese encephalitis each year

~59,000

deaths from rabies each year

Vaccines

Japanese encephalitis, tick-borne encephalitis, measles, mumps, rubella, varicella and zoster.

After an animal bite

Wash the wound for 15 minutes; vaccine, and immunoglobulin when indicated.

Vectors and travel

Repellents, nets and vector control. Pre-travel advice for endemic areas.

World Health Organization fact sheets: Japanese encephalitis; Rabies.

PART 7

Take home

Ten rules, then the answers to the three questions.

TAKE HOME

Ten rules

1. Fever with a brain that is not working is encephalitis until shown otherwise
2. Aciclovir within 6 hours; it waits for nothing
3. Lumbar puncture early; CT first only for signs of brain shift
4. A negative early HSV PCR is repeated, not trusted
5. A multiplex panel does not replace specific PCR
6. MRI within 24 hours; the location names the cause
7. Under 3 months, psychiatric, with seizures or movements: think autoimmune
8. Treat autoimmune encephalitis on criteria, not on the antibody
9. Relapse after HSV: test for NMDA receptor antibodies
10. Survival is not recovery: plan the rehabilitation

PRE-TEST · ANSWER 1

The negative PCR

B **Continue aciclovir and repeat the lumbar puncture in 2–3 days**

HSV PCR can be negative in the first 72 hours of illness. With a compatible CSF and mesial temporal signal on MRI, treatment continues and the puncture is repeated. Empirical aciclovir stops only when the PCR is negative and the clinical picture, CSF and imaging do not support HSV.

Granerod J, et al. EAN–ESCMID guideline. Eur J Neurol 2026.

PRE-TEST · ANSWER 2

The psychiatric ward

B **CSF NMDA receptor antibodies, with pelvic imaging**

Psychosis, then dyskinesias, seizures and autonomic instability in a young woman is anti-NMDA receptor encephalitis until excluded. MRI is normal in about two thirds. CSF is more sensitive than serum, and an ovarian teratoma must be sought. Thyroid peroxidase antibodies are common in healthy people and prove nothing.

Titulaer MJ, et al. Lancet Neurol 2013. Gresa-Arribas N, et al. Lancet Neurol 2014. Flanagan EP, et al. JAMA Neurol 2023.

The steroid question

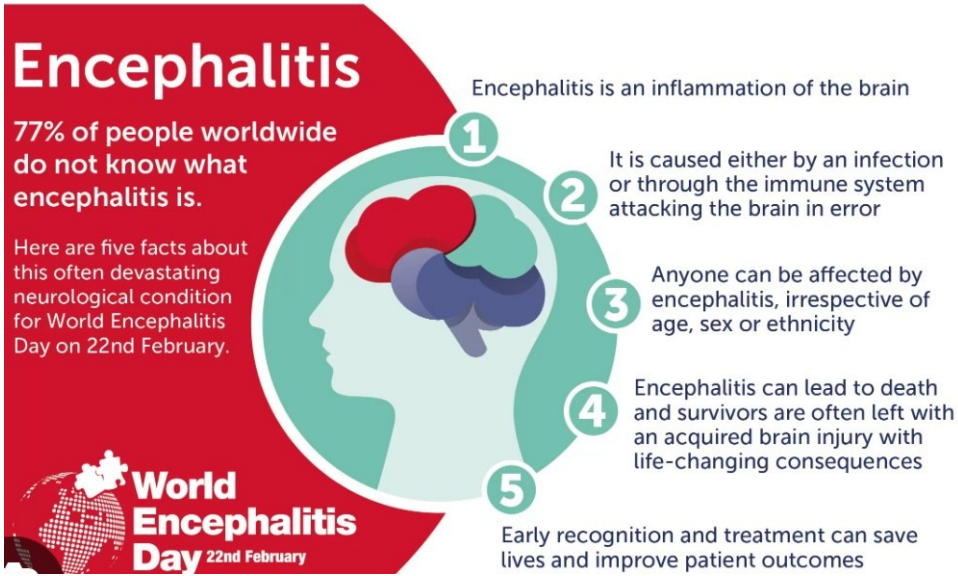
C **No proven benefit; neither for nor against; appears safe**

DexEnceph randomised 94 adults with HSV encephalitis to aciclovir with or without dexamethasone. Verbal memory at 26 weeks did not differ, and there was no safety signal. The EAN–ESCMID guideline makes no recommendation for or against, and notes that steroids given empirically for another suspected cause are unlikely to be harmful.

Solomon T, et al. Lancet Neurol 2026. Granerod J, et al. Eur J Neurol 2026.

TAKE HOME

22 February



World Encephalitis Day. Encephalitis International.

77%

of people worldwide do not know what encephalitis is.

Teaching it is part of treating it.

References

1. Granerod J, et al. Diagnosis and management of infectious encephalitis in adults: guidelines from the EAN and ESCMID. Eur J Neurol 2026. doi:10.1111/ene.70647

2. Solomon T, et al. Adjunct dexamethasone in adults with herpes simplex virus encephalitis (DexEnceph). Lancet Neurol 2026.

3. Venkatesan A, et al. Case definitions, diagnostic algorithms and priorities in encephalitis. Clin Infect Dis 2013;57:1114–1128.

4. Tunkel AR, et al. The management of encephalitis: IDSA guidelines. Clin Infect Dis 2008;47:303–327.

5. Solomon T, et al. Management of suspected viral encephalitis in adults: ABN and BIA guidelines. J Infect 2012;64:347–373.

6. Granerod J, et al. Causes of encephalitis and differences in their clinical presentations in England. Lancet Infect Dis 2010;10:835–844.

7. Whitley RJ, et al. Vidarabine versus acyclovir therapy in herpes simplex encephalitis. N Engl J Med 1986;314:144–149.

8. Raschilas F, et al. Outcome of and prognostic factors for herpes simplex encephalitis. Clin Infect Dis 2002;35:254–260.

9. Gnann JW, et al. Herpes simplex encephalitis: lack of clinical benefit of long-term valacyclovir. Clin Infect Dis 2015;61:683–691.

10. Armangue T, et al. Frequency, symptoms, risk factors and outcomes of autoimmune encephalitis after herpes simplex encephalitis. Lancet Neurol 2018;17:760–772.

11. Graus F, et al. A clinical approach to diagnosis of autoimmune encephalitis. Lancet Neurol 2016;15:391–404.

12. Dalmau J, Graus F. Antibody-mediated encephalitis. N Engl J Med 2018;378:840–851.

13. Titulaer MJ, et al. Treatment and prognostic factors for long-term outcome in anti-NMDA receptor encephalitis. Lancet Neurol 2013;12:157–165.

References, continued

14. Gresa-Arribas N, et al. Antibody titres at diagnosis and during follow-up of anti-NMDA receptor encephalitis. Lancet Neurol 2014;13:167–177.

15. Schmitt SE, et al. Extreme delta brush. Neurology 2012;79:1094–1100.

16. Abboud H, et al. Autoimmune encephalitis: proposed best practice recommendations. J Neurol Neurosurg Psychiatry 2021;92:757–768.

17. Pollak TA, et al. Autoimmune psychosis: an international consensus. Lancet Psychiatry 2020;7:93–108.

18. Flanagan EP, et al. Autoimmune encephalitis misdiagnosis in adults. JAMA Neurol 2023;80:30–39.

19. Odaka M, et al. Bickerstaff's brainstem encephalitis: clinical features of 62 cases. Brain 2003;126:2279–2290.

20. World Health Organization. Fact sheets: Japanese encephalitis; Rabies.

21. Marr JS, Calisher CH. Alexander the Great and West Nile virus encephalitis. Emerg Infect Dis 2003;9:1599–1603.

22. Whitley RJ, et al. Adenine arabinoside therapy of biopsy-proved herpes simplex encephalitis. N Engl J Med 1977;297:289–294.

23. Pollak TA, et al. and Dalmau J, et al. as cited on slides; Cahalan S. Brain on Fire. Free Press, 2012.

24. Dodd KC, et al. Periprocedural antithrombotic management for lumbar puncture: Association of British Neurologists clinical guideline. Pract Neurol 2018;18:436–446.

25. McGill F, et al. The UK joint specialist societies guideline on the diagnosis and management of acute meningitis and meningococcal sepsis in immunocompetent adults. J Infect 2016;72:405–438.



Thank you

Questions, corrections and cases are welcome.

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