LRI Children's Hospital

Encephalitis in Children & Young People

Staff relevant to:	Clinicians and Health Professionals working within UHL Children's Hospital assessing and managing children and young people aged between 1 month and 18 years with suspected or proven encephalitis.
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Written by: Reviewed by:	R Radcliffe, D Baskaran, U Patel, D Baskaran, Oliver Toovey, R Radcliffe,
Trust Ref:	C21/2014

1. Introduction and Who Guideline applies to

This guideline is for Clinicians and Health Professionals assessing and managing children and young people aged between 1 month and 18 years with suspected or proven encephalitis.

Please take additional advice in immunocompromised children and those with a history of travel.

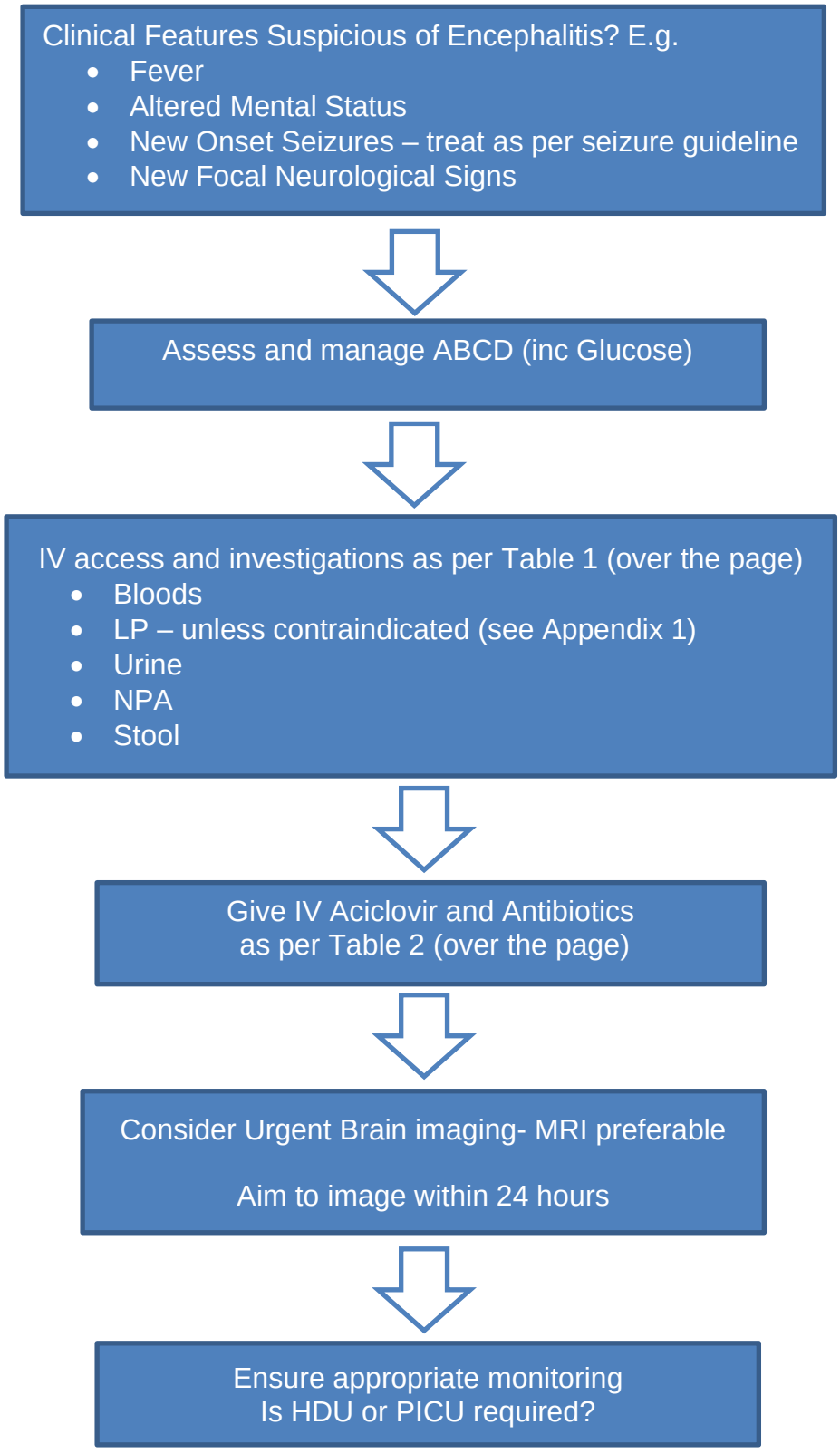
Encephalitis is a rare (2.8/100 000) but potentially devastating neurological condition with many causes. Prompt diagnosis and appropriate management significantly reduces morbidity and mortality.

Contents

Related Guidelines:

- **Neonatal Herpes Simplex UHL Childrens Medical Guideline**
- **Meningitis UHL Childrens Medical Guideline**
- **Sepsis UHL Childrens Hospital Guideline**
- **Lumbar Puncture UHL Childrens Hospital Guideline**
- **Decreased Consciousness UHL Childrens Hospital Guideline**

Initial Management of Suspected Viral Encephalitis



Key:
LP – Lumbar Puncture
NPA – Nasopharyngeal Aspirate
HDU – High Dependency Unit
PICU – Paediatric Intensive Care Unit

Table 1 – Initial Investigations for suspected Encephalitis (detailed history is required in all cases including travel history, immune status etc.)

Bloods	FBC, Clotting, UE, LFT, Ammonia, Lactate, Gas, Blood Culture, Serology for EBV, CMV, Mycoplasma Consider HIV screening: after counselling Glucose with LP Serum to be paired with CSF to be stored in virology^
CSF **(Send ≥10 drops in all 3 bottles + grey blood bottle)**	Opening pressure (but don't delay LP or treatment) Gram Stain and Culture, Glucose, Protein, Lactate. PCR for HSV/VZV/Enterovirus/Adenoviruses - The virology laboratory will freeze excess CSF not used for initial investigations so further tests can be added on later upon request if there is sufficient sample remaining*
Urine **(1st urine passed)**	Culture Organic/Amino acids/toxicology
NPA	PCR for Respiratory viruses, Enteroviruses and Adenoviruses Consider atypical pneumonia PCR for mycoplasma
Stool	Enterovirus RNA PCR (if CSF negative)
Radiology **(Within 24 hours if stable)**	MRI or CT if MRI unavailable Sedation is contraindicated, consider GA if necessary
Electroencephalogram (EEG)	Helps to differentiate encephalitis from non-convulsive status epilepticus activity (i.e. Focal or absence seizure)

^In rare circumstances, where clinical picture does not improve or suggestive of other possible conditions, sample storage can be helpful.
* If an unusual cause is suspected/possible due to eg. Travel history, immunosuppressed status, consider sending extra CSF for save in the virology lab

Table 2 – Empirical treatment for suspected Encephalitis*

Age	**Treatment**
28 days - <3 months	Aciclovir 20mg/kg IV TDS Ceftriaxone 80mg/kg OD Amoxicillin 50mg/kg QDS
3 months – <12 years	Aciclovir 500mg/m2 IV TDS Ceftriaxone 80mg/kg OD
12 years onwards	Aciclovir 10mg/kg IV tds Ceftriaxone 80mg/kg OD

*Give with empirical treatment for bacterial meningitis.

- For Infants < 28 days, please see **Neonatal Herpes Simplex UHL Childrens Medical Guideline**

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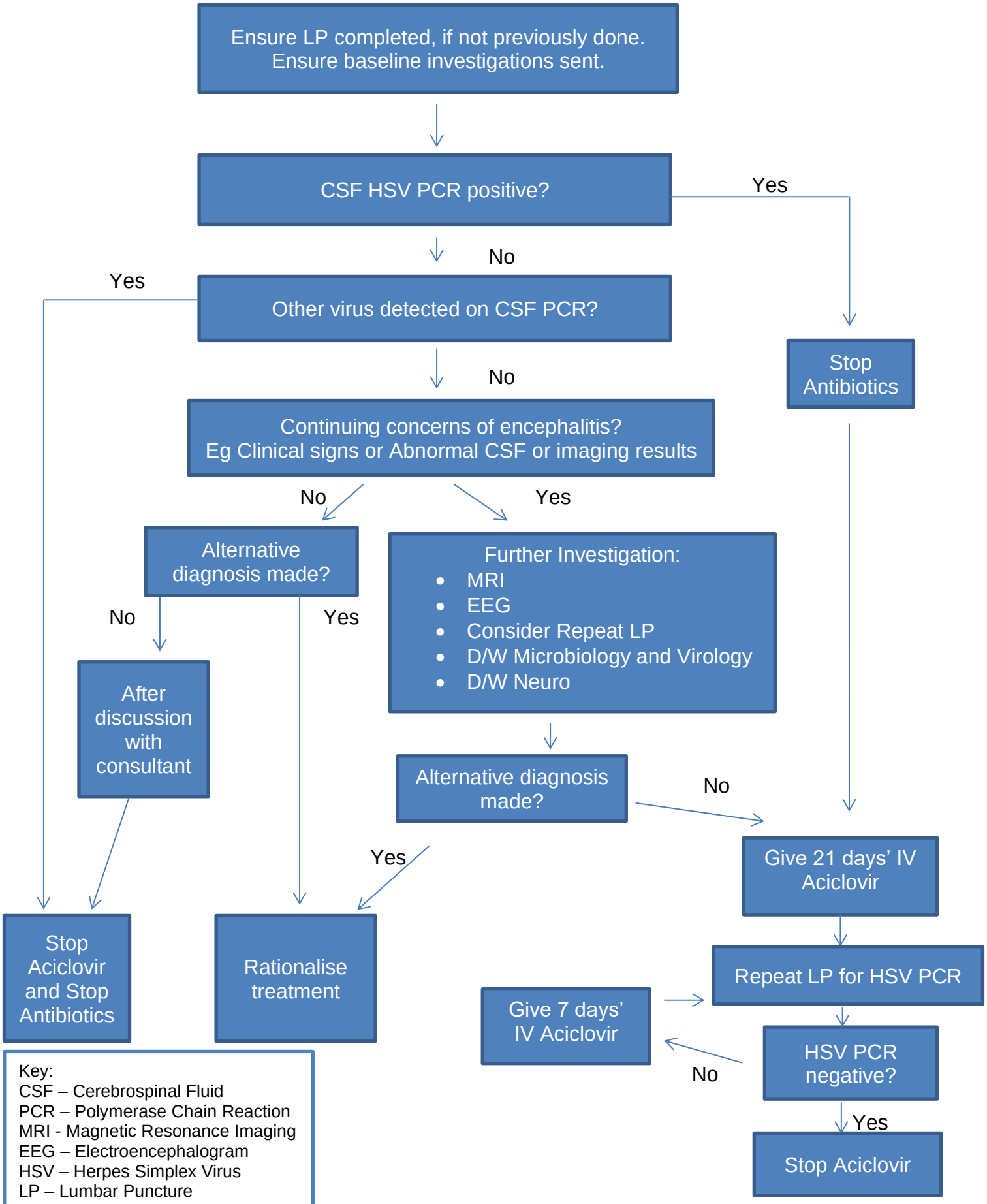
On-going management of suspected Encephalitis



Key:
CSF – Cerebrospinal Fluid
PCR – Polymerase Chain Reaction
MRI - Magnetic Resonance Imaging
EEG – Electroencephalogram
HSV – Herpes Simplex Virus
LP – Lumbar Puncture

2. Guideline standards & procedures

2.1 Signs and Symptoms:

These can be non-specific, especially in a young child, but include:

- Fever or temperature instability
- Headache
- Altered level of consciousness
- Nausea or vomiting
- Seizures
- Focal neurological signs
- Altered behaviour

The 2014 consensus statement of the International Encephalitis Consortium proposed the following **diagnostic criteria** for encephalitis:

1. Altered mental status (i.e. decreased or altered level of consciousness, lethargy, or personality change) lasting ≥24hrs with no alternative cause identified,

Plus

2. 2 of the following for a "possible diagnosis" or ≥ 3 of the following for a "probable diagnosis" :

    a. Documented fever ≥ 38 °C within 72hrs (before or after) presentation
    b. Generalized or partial seizure not fully attributable to pre-existing seizure disorder
    c. New onset focal neurologic findings
    d. CSF WBC count ≥ 5 cells/microL
    e. Abnormality of brain parenchyma on Neuroimaging suggestive of encephalitis that is new or appears have acute onset
    f. Abnormality that is consistent with encephalitis and not attributable to another cause.

In an older child the classical triad of fever, headache and altered conscious level may be more apparent.

Consider a diagnosis of encephalitis when treating for meningitis.

- Other causes of a reduced level of consciousness and appropriate management are covered in the **Decreased Consciousness UHL Childrens Hospital Guideline** C66/2019

2.2 Causes:

More commonly include:

- Herpes Simplex Virus 1 and 2 (most common)
- Enteroviruses (e.g. echoviruses, coxsackie viruses, polioviruses, EV 71)
- Varicella Zoster Virus
- Respiratory Viruses (e.g. Influenza, RSV)
- Adenovirus
- Mycoplasma pneumoniae

Less common pathogens to consider:

- Measles, Mumps and Rubella (can occur even if immunised)
- TB
- In returning travellers consider malaria, arboviruses, e.g. tick borne encephalitis, Japanese encephalitis, West Nile virus and tuberculosis
- In the immunocompromised consider Cytomegalovirus (CMV), Epstein-Barr Virus (EBV) and Human Herpes Viruses 6&7 (HHV-6 and HHV-7) amongst others.
- HIV

Consider post infectious encephalitis (ADEM) if there is sub-acute onset and absence of fever with neurological manifestations. Autoimmune encephalitis should be considered in children presenting with psychiatric symptoms, abnormal movements, seizures, autonomic instability and hypoventilation.

2.3 Clinical Assessment:

A Summary flow chart is found PAGE 3 of this guideline.
Use an ABCDE approach.
Involve PICU if GCS<8 or AV**P**U, raised intracranial pressure or shock evident.

Assess for skin lesions (HSV/ VZV), respiratory symptoms, travel and immunisation status. Be aware that reactivation of HSV is the most common mechanism (and therefore no skin lesions will be found) and that mycoplasma encephalitis may not be associated with a respiratory illness.

2.4 Investigations:

See Table 1, page 4

Also consider if additional investigations for meningitis/sepsis or encephalopathy are necessary. Consult relevant guidelines.

An LP is essential for microbiological diagnosis. Only delay if contraindicated. See tables in appendix for contraindications to and interpretation of LP.

Viral Encephalitis can be associated with raised lymphocytes or polymorphs and a raised protein level. However, the CSF may be normal in the early stages.
Presence of RBCs in CSF can indicate HSV encephalitis

2.5 Empirical Treatment:

See Table 2, page 4

Aciclovir should be started in all patients with clinical features suggestive of encephalitis as soon as possible, pending the results of diagnostic studies.

The diagnosis of herpes simplex encephalitis (HSE) should be considered in any patient with fever and a progressively deteriorating level of consciousness, focal seizures or focal neurological abnormalities in the absence of any other cause.

Other Organisms
In certain circumstances treatment for the following may be considered.

Mycoplasma – the role of antibiotic treatment remains unclear, as this is likely to be an immune mediated response. Treatment with azithromycin (or Clarithromycin if IV route necessary) may be considered.

Influenza –There is very little data available for the treatment of influenza encephalitis.
Oseltamivir may be given for 5 days.

2.6 When NOT to start aciclovir in children with neurological symptoms/signs:

- Child with simple febrile convulsions
- Seizures without documented fever or history of fever (unless immunocompromised)
- Other obvious cause for symptoms, e.g., blocked VP shunt, child with epilepsy (who has an increase in seizures with a febrile illness),
- Acute head injury, drug overdose
- CSF and clinical picture are highly suggestive of bacterial meningitis

2.7 Acute Monitoring:

- Initially ½ to 1 hourly observations for first 4 hours, 2 hourly for next 8 hours then if child is stable can move to 4 hourly. These should include PEW scoring and neuro observations.
- Always consider if this child requires observation on HDU or PICU rather than the ward.
- Aim to keep systolic blood pressure in the high normal range to maintain cerebral perfusion.

2.8 On-going Management:

Close monitoring on the ward is necessary to diagnose and promptly manage of fluid balance disturbance, shock, seizures, raised intracranial pressure or deteriorating conscious level.

Please ensure the responsible consultant is aware of any deterioration.

Further Investigation:

- Consider an EEG, this may help with diagnosis or reveal subtle seizures requiring treatment.
- MRI - if not done acutely. May require a GA as sedation is not recommended.
- **LP - if not done acutely. Also note that CSF can be normal and HSV PCR negative early in the course of HSV encephalitis. Therefore, if clinical suspicion continues and 1st LP was done within 72hrs of onset of illness, then a repeat LP with viral PCR is recommended.**

Consider siting a long line early in treatment, as the treatment course for HSV Encephalitis is 21 days

It may be possible to combine a GA for the above procedures if necessary.

2.9 When to stop aciclovir in children treated for suspected HSV encephalitis:

If there is no on-going clinical suspicion of HSE e.g. -
A definitive alternative diagnosis/organism becomes apparent, or it seems very unlikely that the patient has viral encephalitis, e.g. a very rapid recovery or aciclovir may not have been indicated at presentation.
Or
If a negative CSF HSV PCR is obtained at >72 h following onset of neurological symptoms
AND
there is a low clinical suspicion of HSE (e.g., a clinical recovery and normal level of consciousness, normal neuroimaging and <5 cells/mm^3 in CSF)

2.10 When NOT to stop aciclovir in children treated for suspected HSV Encephalitis:

Negative CSF HSV PCR but other features consistent with HSE (particularly if CSF and MRI findings are abnormal and consistent with the diagnosis). CSF pleocytosis can be absent and false negative HSV PCR results can occur, particularly early in the illness (<72hrs).

2.11 Notification

Viral encephalitis is a notifiable disease. Please notify routinely to the UK Health Security Agency. They can be contacted via switchboard.

The referral form can be found at
https://www.gov.uk/government/publications/notifiable-diseases-form-for-registered-medical-practitioners

2.12 Treatment courses:

HSV encephalitis - suspected or proven, 21 days of IV aciclovir at the above doses should be given.
A negative PCR at the end of treatment is associated with better outcome. In PCR positive patients repeat the LP towards the end of treatment and continue if remains positive - Please refer table on page 6 for more clarification if required.
Please monitor renal function and neutrophil count during treatment.
There is no place for the use of oral aciclovir as CSF penetration is poor.

VZV encephalitis – 10-14 days of IV aciclovir (Cerebellitis -no specific treatment required). The evidence is unclear about repeating the LP at the end of treatment. If there are cases requiring further management, discussion with virology would be recommended.

Influenza encephalitis - Consider 5 days of oseltamivir at standard doses.

Mycoplasma associated encephalitis – Consider treatment with Azithromycin (or Clarithromycin if IV route necessary) if severe.

No treatment is generally recommended for Enterovirus or adenovirus meningitis.

For other infectious aetiologies, immunocompromised patients or travellers, please seek specialist advice from virology/microbiology.

Further information on rarer aetiologies and treatment can be found in: References 2 and 3

2.13 Prognosis and Follow up:

Long term neurodevelopmental morbidity probably depends on the infectious agent but is as high as 60% in survivors. Focal neurology, encephalopathy, CSF pleocytosis and abnormalities on neuroimaging may be associated with persistent sequelae. Seizures at presentation are not predictive of prognosis at discharge.

Follow up should be tailored to a child's needs on discharge, with appropriate neurodevelopmental follow up with the MDT if necessary. If no concerns are identified at discharge, all children should receive a general paediatric follow up in 6-8 weeks.

3. Education and Training

None required

4. Monitoring Compliance

What will be measured to monitor compliance	How will compliance be monitored	Monitoring Lead	Frequency	Reporting arrangements
Adherence to guideline standards	Audit	R. Radcliffe	5 yearly	Departmental audit meeting

5. Supporting References

1. Drug doses- BNF-c
2. Encephalitis in Children. Thompson C, Kneen R, Riordan A, et al. Arch Dis Child (2011)
3. Management of suspected viral Encephalitis in children: Association of British Neurologists and British Paediatric Allergy, Immunology and Infectious Diseases Group National Guidelines. Kneen R, Michael BD, et al. Journal of Infection (2012)
4. The Management of Encephalitis: Clinical Practice Guidelines by the Infectious Diseases Society of America. Tunkel A, Glaser C, Block K, et al. CID (2008)
5.Acute viral encephalitis in children : Clinical manifestations and diagnosis- UpToDate

6. Key Words

Altered Mental Status, Fever, Seizures, Neurological

The Trust recognises the diversity of the local community it serves. Our aim therefore is to provide a safe environment free from discrimination and treat all individuals fairly with dignity and appropriately according to their needs.
As part of its development, this policy and its impact on equality have been reviewed and no detriment was identified.

CONTACT AND REVIEW DETAILS	
Guideline Lead (Name and Title) R. Radcliffe - Consultant	**Executive Lead** Chief Nurse
Details of Changes made during review: October 2024 **1.** Added author names: Ushma Patel, Oliver Toovey **2.** Associated guidelines referral links changed from insite to UHL connect **3.** In table 1 for Investigations on page 4: edited NPA section to consider atypical pneumonia PCR for mycoplasma. Also, added information about extra CSF and serum to preserve in virology **4.** Clarification on continuing treatment on page 11: Evidence about repeating LP and further treatment in cases of HSV encephalitis and VZV encephalitis **5.** Contraindications to LP in Appendix 1 on page 13: hyperlinked to existing guidelines for LP in children from UHL Children Hospitals	

Appendix 1 – Contraindications to LP- refer to Lumbar puncture UHL Children Hospital Guidelines