PedsCases Podcast Scripts

This podcast can be accessed at www.pedscases.com, Apple Podcasting, Spotify, or your favourite podcasting app.

ENCEPHALITIS

Developed by Emily Kacer and Dr. Brandon Meaney for PedsCases.com.
May 2025

Introduction:

Welcome to PedsCases and thank you for listening to this podcast. Our episode today will cover an approach to encephalitis in the pediatric population. My name is Emily Kacer and I am a first-year pediatrics resident at McMaster University in Hamilton, Ontario. This episode was developed with the support and guidance of Dr. Brandon Meaney. Dr. Meaney is the Division Head of Pediatric Neurology and an Associate Professor of Pediatrics at McMaster University. In his clinical practice, he supports children with a variety of neurologic conditions including epilepsy, movement disorders, and developmental delay with an academic focus in medical education.

The objectives for today's episode are as follows:

1. Define encephalitis and identify the common infectious and autoimmune causes in the pediatric population.
2. Discuss an approach to the diagnosis of encephalitis including clinical presentation and investigations.
3. Compare and contrast encephalitis with meningitis.
4. Outline an initial approach to the management of encephalitis.
5. Review some of the potential long-term complications of encephalitis.

Clinical Cases:

Let's begin our episode with a clinical scenario. You are a third-year clinical clerk on your emergency medicine core rotation in a rural setting that is over 45 minutes away from the nearest pediatric hospital. You are asked by your preceptor to go see the next two patients. Your first patient is Jameel, a 4-year-old male, presenting with 3 days of fever and a rash. His parents are particularly concerned because he has become unbalanced in his walking and has seemed to stop talking over the last day or so. He has generally not been acting like his normal energetic self and has been very fatigued. You begin to wonder what may be causing his rash and lack of energy. What other symptoms would you want to ask about during your history with Jameel and his parents? What features are important to assess on physical examination?

Before you visit Jameel, you learn about your second patient by reviewing the triage nurse's note. Skylar is a 15-year-old female brought in by her parents due to bizarre behaviour over the

past 5 days. Despite her recovery from a flu-like illness in the last week, Skylar has been very irritable and acting uncharacteristically aggressive toward her parents and younger siblings. Yesterday, her father saw her talking, as though to someone, despite being alone in her bedroom. Skylar's parents worry that she may be experimenting with substances due to peer pressure and are concerned by this out of character behaviour. Considering Skylar's new onset of hallucinations and abnormal behaviour, you wonder if this could be a first episode of psychosis. What other organic causes of hallucinations would be important to consider in your differential diagnosis? How would you approach asking Skylar about her recent changes in behaviour?

Although these cases may initially appear unrelated, there are several similarities between the acute and complex presentations of Jameel and Skylar. We will revisit these cases and their etiologies at the end of today's episode.

1. Defining encephalitis

Firstly, what is encephalitis? Breaking the word down, the '-itis' suffix informs us that there is some kind of inflammatory process occurring while the root of the word 'encephalo-' refers to the brain. Compared to the term 'meningitis' which refers to the inflammation of the meninges, encephalitis is inflammation specifically affecting the brain parenchyma (1). There can be, and often is, some overlap between these two inflammatory states due to the proximity of these anatomical structures. Hence sometimes the term meningoencephalitis is used to describe the situation when both the meninges and the brain parenchyma are involved in the inflammatory process.

Now that we've clarified that encephalitis is inflammation of the brain, how does it differ from the term encephalopathy? As we now know, 'encephalo-' refers to the brain and the suffix '-pathy' refers to a diseased state. If you're anything like me, you'll recognize that brain disease is a vague definition for a term that is used so often in medicine. For our purposes, we can think of encephalopathy as an acute change to a child's behaviour, responsiveness, and/or sensorium that does not necessarily involve direct brain inflammation. Other causes of encephalopathy, beyond encephalitis, may also include ischemia, medications, or metabolic changes (1,2).

This understanding brings us to our more complete definition of encephalitis as a type of acute encephalopathy where children present with neurologic dysfunction due specifically to inflammation of the central nervous system (1).

Now that we've hopefully clarified the term encephalitis, what are some of the common causes of this 'acute brain inflammation' within pediatric populations? Broadly, we can think of encephalitis as being either viral or autoimmune in origin (3). While there can be other infectious and non-infectious causes, they are quite rare and outside of the scope of what most medical learners would encounter in their practice (1).

Viral encephalitis can occur when a virus directly invades the central nervous system or the CNS (1). Even after the viral infection has resolved, long-term changes can occur due to the local immune response which affects neurons, astrocytes, and microglia (4).

When we look at the viral causes of encephalitis, we can further subdivide these infectious agents into two categories: herpes simplex virus, or HSV, and every other virus. We make this

distinction because HSV-1 and HSV-2 are common causes of viral encephalitis and, more importantly, have a very specific management approach.

We could spend an entire podcast episode discussing all the different possible viral etiologies of encephalitis. Some notable agents include influenza, Epstein-Barr virus, cytomegalovirus, and enterovirus (1,2). A patient's travel history may also be used to inform potential viral etiologies of encephalitis based on geographic distribution. Fortunately, with the introduction of vaccines, encephalitis caused by polio, measles, and other vaccine preventable viruses has declined in prevalence. At our tertiary children's hospital, which serves a population of approximately 2.5 million Ontarians, we see around 1-3 cases of viral encephalitis each month.

HSV-1 is the single most common viral etiology for encephalitis across all age groups whereas HSV-2 tends to primarily affect neonates (1). Broadly we need to consider Herpes in all children that present with signs and symptoms of encephalitis because of the substantial morbidity and mortality associated with delayed treatment (2).

Turning to non-infectious causes of encephalitis, these are often autoimmune presentations (5). Most commonly, we see N-methyl-D-aspartate, or NMDA, receptor antibody mediated encephalitis which targets neuronal synapses and the ability of messages to be sent across neurons (3,6,5). This is the most common autoimmune encephalitis. It is usually associated with a preceding viral infection, which can be described as a post- or para-infectious process. Rarely, the autoimmune process can be a paraneoplastic phenomenon triggered by an underlying malignancy such as an undiagnosed ovarian tumor. A different type of autoimmune encephalitis is known as acute disseminated encephalomyelitis, or ADEM, where the inflammation is targeted toward the conductive white matter. This post-infectious autoimmune condition is characterized by demyelination of the brain as well as potentially of the spinal cord (3,7).

Broadly, autoimmune encephalitis can develop when antibodies are directed against cell-surface or synaptic proteins. They may also be triggered by underlying conditions including an infection, malignancy, or systemic autoimmune disorder (2,6,5).

Although in some cases we can identify antibodies against specific receptors or ion channels, other presentations have no associated antibodies, and autoimmune encephalitis must be made as a diagnosis of exclusion (6).

While these may sound complex and exceedingly rare, autoimmune encephalitis occurs at a rate higher than any one viral cause of encephalitis in the United States of America (2). For instance, anti-NMDA receptor encephalitis occurs at a rate four times that of HSV-1 (4). Like most other autoimmune conditions, females are more often affected by autoimmune encephalitis (6).

In summary, we have both infectious and non-infectious causes of encephalitis. The single most common infectious cause is HSV whereas the most common autoimmune encephalitis is anti-NMDA receptor encephalitis.

2. Diagnosis of encephalitis

Now that we have a basis of the etiologies of encephalitis, how do we identify encephalitis in a pediatric patient? The clinical presentation requires two components: acute encephalopathy and

evidence of inflammation in the CNS (1). Generally, we can think about this as the information we gather on history and physical examination which will be used to inform our understanding of the encephalopathy. Our subsequent investigations are what enable us to confirm the presence of CNS inflammation.

Eliciting a clear timeline on history is crucial as encephalitis requires an acute alteration in mental status over at least the past 24 hours (1,8). Revisiting our timeline, infectious causes present more acutely whereas autoimmune encephalitis tends to be more subacute in nature and often is diagnosed later into the disease course (2,4,5). Children may present with a decreased level of consciousness, irritability, agitation, or other changes in behaviour (1,8,2). In younger infants, this presentation can be even more non-specific, and the only signs of encephalitis may be poor feeding or lethargy. In older children, we may see more psychiatric presentations including labile or fluctuating emotions, temper tantrums, or even acute psychosis (8,2,6). The presence of clear psychiatric manifestations and/or memory changes should increase our suspicion of autoimmune encephalitis (2,5,6).

Beyond these changes to mental status, we may also see new onset seizures and focal neurological deficits (3). For instance, impairments to sensory or motor function may present as speech disorders, weakness, cranial nerve palsies, or ataxia (1,8,3). We may also see disturbances to autonomic function (3,2).

Often, affected children will have a headache, fever, nausea, vomiting, or fatigue (3,1,4). If we suspect an infectious etiology, we should inspect for rashes, such as the characteristic vesicular lesions of HSV (8,2). Additionally, it is important to inquire about respiratory involvement, gastrointestinal manifestations, and urinary symptoms (8).

On history, we also want to ask about recent travel, exposures to insect bites or animals, and immunization history to determine if less common etiologies of encephalitis should be considered (8). Generally, we want to prioritize investigations for the most common and treatable causes of encephalitis but use risk factors, such as a lack of childhood immunizations, to determine if we should order additional investigations (2). It is also important to ask about recent infections to identify a possible preceding illness or prodrome for autoimmune encephalitis (5).

Before beginning the physical examination, we always want to check vitals, use the ABCDE approach, and perform a brief cardiorespiratory examination to ensure our patient is stable. With severe encephalitis, we can see status epilepticus, vital instability due to autonomic involvement, and cerebral edema. Once confirming the clinical status of our patient, we want to perform a thorough neurological examination with particular attention to motor, sensory, cerebellar, reflex, and cranial nerve function. Are there any signs of focal neurologic deficits? Conducting a mental status examination can also be beneficial to assess psychiatric symptoms (5,8).

Although encephalitis is largely a clinical diagnosis, objective findings of CNS inflammation can be obtained via lumbar puncture, neuroimaging, or electroencephalography, known as an EEG (1). When performing the lumbar puncture, we want to record opening pressure and obtain a sample for cell counts and differentials, bacterial gram staining, culture, and viral polymerase chain reaction or PCR (8,2). We can also order an autoimmune encephalitis panel which can

identify antibodies for NMDA receptors and other common autoantibodies (8,5). Findings suggestive of encephalitis include cerebrospinal fluid pleocytosis or increased white blood cells, and elevated protein, as these results are consistent with inflammation (3,4,2,7). Also, if there are any signs of increased intracranial pressure, such as asymmetric pupils, papilledema, focal neurologic signs, Cheyne Stokes breathing, headaches, focal seizures, or reduced level of consciousness, we should always perform neuroimaging first before a lumbar puncture. We want to ensure there is no risk of herniation before performing the lumbar puncture and in some cases, we may need to initiate treatment before the lumbar puncture (8,3).

If suspecting an infectious etiology, we would order serologies including HSV, varicella zoster virus, Epstein-Barr virus, and cytomegalovirus (3,8). It is also reasonable to consider a respiratory panel, urinalysis, and stool sample for culture if suspecting an infectious origin. Furthermore, we can test for autoantibodies in the serum if suspecting an autoimmune cause (2). More general laboratory tests include a complete blood count, electrolytes, glucose, and blood cultures which may also help inform the clinical picture (8).

Supportive findings on neuroimaging or EEG can also provide objective evidence of CNS inflammation (3). When conducting our neuroimaging, it is important to remember that there may not be any imaging signs of encephalitis at the time of presentation. If present, parenchymal findings can provide another piece of clinical insight. Non-specific findings may include brain edema, but specific findings may be present depending on the etiology (8). For instance, in ADEM, we may see multifocal white matter lesions whereas in HSV, we tend to see temporal lobe localization on the MRI (7,3,2,8). Generally, we prefer MRI to CT due to the decreased radiation exposure and increased accuracy, but CT is often more readily available and can be helpful to rule out high intracranial pressure or other neurosurgical emergencies. Similarly to neuroimaging, any findings obtained via EEG may be non-specific or this study may be entirely normal (8,2,4).

In summary, we want to assess for the presence of acute encephalopathy with our history and physical exam while our findings from the laboratory studies, infectious workup, lumbar puncture, neuroimaging, and EEG provide supportive findings for this largely clinical diagnosis.

3. Encephalitis vs meningitis

If you are anything like me, you likely had some confusion about the differences between encephalitis and meningitis. Both involve inflammation either near or within the CNS which can be hard to differentiate. Circling back to our initial definition, encephalitis is inflammation of the brain. Breaking down the term meningitis, the meninges are protective membranes that cover and make direct contact with the surface of the brain. This anatomical distinction is important because the clinical presentations can have a lot of overlap. If you're interested in learning more about meningitis, there is an excellent infographic and podcast episode on the PedsCases website. To contrast the presentation of meningitis with encephalitis, we will discuss it briefly in today's episode.

Most commonly, we see inflammation of the meninges due to a viral or bacterial infection. Viral pathogens of meningitis are very similar to those of viral encephalitis and include HSV, enterovirus, varicella zoster virus, Epstein-Barr virus, and cytomegalovirus (9). These agents tend to start in the respiratory or gastrointestinal tract and travel to other regions of the body,

including the meninges. Bacterial agents often reach the meninges by one of two major mechanisms:

1. Spreading from a bacteremia
2. Colonizing nearby structures to their entry points, such as the sinuses or mastoids

Less commonly, bacteria may access the meninges after a traumatic injury or through medical devices including cerebrospinal fluid shunts.

The most common pathogens causing bacterial meningitis include Group B *Streptococcus* and *Escherichia coli* for infants below the age of 3 months whereas any children older than 3 months tend to be infected by *Streptococcus pneumoniae* or *Neisseria meningitidis* (10).

In both viral and bacterial meningitis, infants tend to present with a fever or hypothermia and non-specific symptoms such as irritability, vomiting, and poor oral intake. Children also frequently have a fever, nausea, and vomiting but they may demonstrate a classic triad of symptoms or meningismus. These symptoms are photophobia, headache, and neck stiffness or nuchal rigidity which may or may not be exhibited but are highly suggestive of meningitis (9-11). Children and infants of any age may also present with lethargy, preceding respiratory or gastrointestinal symptoms, seizures, signs of increased intracranial pressure (such as a bulging fontanelle), and systemic manifestations including sepsis (9,10). Specific to viral meningitis, we may see associated rashes or conjunctivitis (11).

Meningitis has unique physical exam findings suggesting meningeal inflammation including nuchal rigidity, Kernig's sign, and Brudzinski's sign. Although, these clinical signs may not be positive in young children and infants. As the meninges directly cover the brain, it is possible to see the progression of meningitis into encephalitis and the primary infection may not be readily apparent due to the presence of both processes occurring (9,11,2).

In the workup of meningitis, we often treat it as if it is bacterial due to the substantial morbidity and mortality associated with this medical emergency. Investigations are fairly similar to those with encephalitis including blood culture, electrolytes, glucose, and creatinine. We also want to obtain a lumbar puncture sample for viral studies, bacterial culture, cell count, and differential. In bacterial meningitis, we tend to see pleocytosis or increased white blood cells in the cerebrospinal fluid. In a viral meningitis, mononuclear elevation is common whereas bacterial meningitis tends to be neutrophil dominant. We also may see low glucose with bacterial meningitis due to the utilization of glucose by bacteria as an energy source (10,11).

Considering how varied the presentation of encephalitis can be; we want to keep our list of differential diagnoses broad. Meningitis is often at the top of the differential due to the overlap in these presentations and the emergent nature of treatment in both conditions. We also want to consider encephalopathy which is a change to neurological function without inflammation (6). We should consider if there has been any history of toxic ingestions, tuberculosis, psychiatric disorders, and mitochondrial conditions as possible etiologies for these acute changes in neurological status (5). We should also assess for possible trauma to the head, status epilepticus, inborn errors of metabolism, stroke, and intracranial masses such as an abscess or malignancy (8,6,2). All these conditions may present similarly to encephalitis and should be considered during our investigations.

Developed by Emily Kacer and Dr. Brandon Meaney, McMaster University for PedsCases.com.
May 2025.

Summarizing our discussion of encephalitis and meningitis, we approach investigations very similarly for both conditions including lumbar puncture, laboratory tests, and infectious workup. Meningitis has classic findings on examination and history due to meningeal inflammation which are not observed with the direct inflammation of the brain that occurs in encephalitis. Clinically, it can be challenging to differentiate these two disease processes and in most cases, we will begin treatment to cover bacterial or viral meningitis and viral encephalitis.

4. Management of encephalitis

Now that we have discussed how to approach a diagnosis of encephalitis, how do we manage a child with suspected encephalitis? First and foremost, we empirically start acyclovir and broad-spectrum antibiotics for infectious encephalitis. Until we can definitively rule out bacterial meningitis, with the results of a lumbar puncture, we want to start on vancomycin and ceftriaxone (3,8,12). This is a major takeaway from today's episode, and it bears repeating as we want to emphasize the importance of initiating acyclovir, vancomycin, and ceftriaxone. These interventions can be lifesaving in the cases of HSV encephalitis or bacterial meningitis. We may discontinue these broad-spectrum treatments once we have the results of the lumbar puncture and possibly the blood culture if indicated (2). Other antibiotics may also be started based on the clinical picture and the child's risk factors before we receive the final results of these investigations (12).

In autoimmune encephalitis, we want to stop the inappropriate immune response and reduce inflammation (13). Generally, this consists of combination of intravenous corticosteroids, immunoglobulins, and possibly plasma exchange (2,6). Other immunomodulators may be used as second line agents but are often done in consultation with pediatric neurology when first line treatments are ineffective (4). Even if we never isolate a particular causal antibody during the clinical course but continue to have a high suspicion for autoimmune encephalitis, we treat using this same approach (6).

We also provide supportive care for electrolyte abnormalities, acid-base disturbances, fluid imbalances, and seizures which may be associated with encephalitis (8,12). For instance, lorazepam may be initiated for seizure abortion (8). Children with increased intracranial pressure, status epilepticus, cardiorespiratory instability, or coma are typically best managed in the intensive care unit due to the high acuity and severity of these presentations in encephalitis (4,12).

Overall, we treat with acyclovir and broad-spectrum antibiotics if suspecting an infectious encephalitis. If autoimmune encephalitis is more likely, we would start treatment to reduce inflammation using intravenous corticosteroids, immunoglobulins, and plasma exchange as possible first line agents.

5. Complications of encephalitis

When considering the prognosis of encephalitis, it is important to acknowledge that we often are unable to identify a specific etiology for viral encephalitis during the acute course (8). For infectious etiologies, most of our predictions for prognosis are based on how sick the child initially presents and what we can visualize with imaging, such as signs of neuronal death (2).

Developed by Emily Kacer and Dr. Brandon Meaney, McMaster University for PedsCases.com.
May 2025.

The specific pathogen may influence prognosis. For instance, most enterovirus meningoencephalitis cases tend to do well with complete recovery whereas children with HSV encephalitis often become very sick with several chronic neurologic sequelae. We know that children often have poorer outcomes if they are younger than 5 years of age, have delayed treatment for HSV encephalitis, or require escalation to ICU level care (12,2). Generally, we see most strides in recovery being made in the first 6 to 12 months of the illness' course (4).

With autoimmune encephalitis, we tend to see a longer time required for recovery and prognostication can be even more challenging, than infectious causes, to associate with neuroimaging findings (2). In the acute phase for both viral and autoimmune encephalitis, we want to avoid immobility as this can lead to loss of function and complications including venous thromboembolism for children (4). Involvement of allied health including physiotherapy, occupational therapy, and/or speech language pathology can also be beneficial depending on the child's presentation and associated neurological deficits (4,2). Neurological consequences of encephalitis are not often initially apparent, and children may present later with a range of symptoms requiring long-term rehabilitation and outpatient treatment (4). For instance, we may see children experience intellectual disability, focal motor deficits, seizures, hearing impairments, learning disabilities, speech disorders, or impaired executive functioning due to the encephalitis (2,12,4). Generally, we can expect 42% of patients to have limited or incomplete recovery to their prior neurological and functional statuses (2).

In summary, the prognosis of both infectious and autoimmune encephalitis can be incredibly challenging to predict, and a child's recovery may not be complete. It is important to ensure that patients are well supported by allied health and pediatric subspecialty services both in hospital and as outpatients.

Clinical Cases:

Revisiting our clinical cases, let's apply what we've learned about encephalitis to determine the best course of action for the management of Jameel and Skylar.

As you'll remember, Jameel is a 4-year-old with an acute onset of fever, fatigue and a rash. He was also more unstable in his walking and had stopped talking. When you meet Jameel and his parents at the bedside, he is asleep. He has a temperature of 38.7 degrees Celsius and is mildly tachycardic but otherwise stable. He awakens when interacted with but is clearly irritable. His parents say that Jameel is normally a very active young boy who loves meeting new people. They initially believed he had a cold that was going around his daycare because of his fever and low appetite. They became increasingly concerned today when he became less responsive and developed a rash around his mouth. During your history, you determine that Jameel has received his routine 18-month vaccinations and is due for his school age vaccinations this upcoming summer. He has not travelled recently and has no known interactions with animals except for his dog who is up to date on all vaccinations. As you perform a review of systems, you notice that his father has a healing cold sore, or herpes labialis, present on his left lower lip. When asked, Jameel's parents disclose that they both have had cold sores throughout their adult years but have never seen similar lesions on Jameel. They have always avoided kissing Jameel whenever they have an active lesion and practice good hand hygiene to avoid passing along their cold sores to their young son.

Upon closer inspection, you see that Jameel's perioral rash is vesicular, erythematous, and clustered with some regions of crusted bleeding. You also note that when Jameel cries, the right side of his mouth doesn't seem to move as much as the left. You point this out to his parents and they agree, saying that they had noticed it earlier today. They have also noted some drooling from the right side of his mouth. They thought this was just related to his skin being sore from the rash.

You find your supervisor to review Jameel's case. You share that you are concerned that Jameel may have HSV encephalitis, because of the constellation of fever, vesicular perioral rash, lethargy, and focal neurologic signs – aphasia and right sided facial weakness. After asking some clarifying questions, she instructs you to call the CT department for urgent neuroimaging as she orders laboratory investigations and calculates the weight-based doses for IV vancomycin, ceftriaxone, and acyclovir. She shares her plans to call the pediatric hospital to facilitate transfer of Jameel and see if any additional testing would be warranted before he travels via ambulance. When you ask if Jameel should have a lumbar puncture as part of his workup, your supervisor explains the risk of significant focal cerebral edema that could be causing a pressure differential. If a lumbar puncture was performed, there could be a significant risk of herniation.

After observing your supervisor discuss the management plan with Jameel's family, you visit Skylar. When you enter the room, Skylar is sitting at the edge of the hospital bed and appears quite agitated. You introduce yourself and explain your role on Skylar's care team to Skylar and her family. You ask Skylar if she feels comfortable with her parents remaining in the room while you discuss what brought her to the hospital and Skylar asks if she can speak with you alone. After confirming the stability of her vitals, Skylar is adamant that she does not need to be in the hospital and that her parents are overreacting. You note that she is speaking rapidly, glancing around at times, and seems distracted. She tells you again that she isn't sick and just wants to go home. She nonetheless agrees to answer some further questions, and endorses that she felt sick last week with a fever, nausea, fatigue, headaches, and muscle aches which led to several missed days of school. She did not experience any respiratory symptoms, loss of appetite, or changes to voiding patterns. Skylar has difficulty recalling some aspects of the history, including if she had any seizures, weakness, or changes to sensation. During your SSHADESS history, you learn that she is not interested in trying any substances despite her peers' use of cannabis and alcohol at parties. She is not yet sexually active but is interested in dating soon. As you finish off your neurological screening examination, you note that she appears to be gazing over your shoulder and appears fearful while staring at the corner of the room. When you ask her what she is looking at, it takes her a few moments to shift her attention back to you, after which she again simply states that she wants to go home. You make a note of this behaviour as part of your mental status examination.

You explain to Skylar that you were hoping to talk with her parents to help with the process of returning to home and she is agreeable to their involvement in her care. You speak with Skylar's parents in the hallway, and they appear quite worried. They corroborate Skylar's history and clarify elements including the timeline of her illness, symptoms experienced, and lack of a prior psychiatric history. During her verbally aggressive episodes, they recall that Skylar screamed at her younger siblings because she thought they had poisoned her food. She refused to eat for the rest of the evening and called her family many cruel names that were completely out of character for Skylar. Her parents are insistent that they do not feel safe with her returning home

until the reason for her strange behaviour is determined. You agree that until more tests are run, Skylar would be safest in the hospital.

You discuss this case with your preceptor and outline your differential which includes first episode psychosis and, although less likely based on your SSHADESS history, substance intoxication or withdrawal. As part of your differential, you highlight the possibility of autoimmune encephalitis due to the prodromal illness last week, Skylar's age, and the subacute course of psychiatric symptoms. Your supervisor agrees with your differential and contacts the nearest children's hospital so that Skylar would have access to child and adolescent psychiatry, pediatric neurology, and general pediatrics care.

During your final evaluation with this preceptor, they share updates on your patients that you saw throughout the rotation. You learn that Jameel's CT demonstrated a region of hypodensity in his left temporal lobe consistent with edema but that no hemorrhage, or mass effect were appreciated. Once it was safe to proceed with a lumbar puncture, his CSF demonstrated a positive viral PCR for HSV-1 as well as elevated white blood cells, normal glucose, and high protein. His cerebrospinal fluid and blood cultures were both negative for bacteria and his broad-spectrum antibiotics were discontinued. He is currently finishing his course of acyclovir. His energy and responsiveness have improved considerably, his facial weakness has resolved, and he has started talking again.

After an extensive workup, including MRI, lumbar puncture, and laboratory investigations, you learn that Skylar was diagnosed with anti-NMDA receptor encephalitis and started on high dose methylprednisolone. Unfortunately, she experienced a cluster of tonic-clonic seizures three days after admission but these were subsequently controlled with anti-seizure medication. She continues to have confusion, intermittent hallucinations and behavioural challenges, and has a long road to recovery ahead, though ultimately it is felt that her prognosis is good. She will be starting further immunosuppressive therapy under the care of pediatric neurology and immunology.

We hope that these cases demonstrate how variable encephalitis presentations can be, both across ages and etiologies.

Summary:

Revisiting some key points from our episode today, we covered the following information:

1. Encephalitis is an acute infectious or autoimmune process leading to central nervous system inflammation and dysfunction. Most commonly, we see HSV as the leading identifiable cause of infectious encephalitis while anti-NMDA receptor encephalitis is the most prevalent autoimmune cause.
2. To diagnose encephalitis, we require evidence of acute neurologic dysfunction and CNS inflammation from our other investigations. Presentations can be highly variable and at times, non-specific, requiring clinical awareness and a thorough workup.
3. The inflammation of the brain parenchyma in encephalitis is anatomically distinct from meningitis which is the inflammation of the meninges. As we discussed, there is

substantial overlap between these clinical presentations and anatomical distribution of the inflammation. As such, meningoencephalitis may be a more accurate description of these conditions. Classically, meningitis presents with photophobia, headache, and nuchal rigidity with Kernig's or Brudzinski's sign on exam.

4. If we suspect encephalitis or meningitis, we should perform a lumbar puncture, when it is safe to do so, and start the child on both broad-spectrum antibiotics and acyclovir to cover the most common infectious etiologies.
5. Outcomes from encephalitis are varied and despite rehabilitation efforts, children may have an incomplete recovery. It is crucial to acknowledge that prompt recognition and treatment of encephalitis can support more favourable prognoses.

Thank you all for listening to today's episode on encephalitis, we hope it was helpful for your learning and made you feel more comfortable with an approach to this presentation in pediatric patients! I also wanted to extend a special thank you to Dr. Meaney for his mentorship and guidance throughout the development of this PedsCases episode.

Developed by Emily Kacer and Dr. Brandon Meaney, McMaster University for PedsCases.com.
May 2025.

References

1. Hardarson HS, Messacar K. Acute viral encephalitis in children: Pathogenesis, epidemiology, and etiology [Internet]. In: Edwards MS, Armsby C, editors. UpToDate; [updated 2022 Dec 5; cited 2024 Jan]. Available from: https://www.uptodate.com/contents/acute-viral-encephalitis-in-children-pathogenesis-epidemiology-and-etiology?search=pediatric%20encephalitis&source=search_result&selectedTitle=3~150&usage_type=default&display_rank=3
2. Fraley CE, Pettersson DR, Nolt D. Encephalitis in Previously Healthy Children. *Pediatr Rev*. 2021;42(2):68-77. doi:10.1542/pir.2018-0175
3. Dean NP, Carpenter JL, Campos JM, DeBiasi RL. A Systematic Approach to the Differential Diagnosis of Encephalitis in Children. *J Pediatric Infect Dis Soc*. 2014;3(2):175-179. doi:10.1093/jpids/piu007
4. Vova JA, Howarth RA. Evaluation, Treatment, and Outcomes of Viral and Autoimmune Encephalitis in Children. *Pediatr Clin North Am*. 2023;70(3):429-444. doi:10.1016/j.pcl.2023.01.007
5. Dalmau K, Rosenfeld MR. Autoimmune (including paraneoplastic) encephalitis: Clinical features and diagnosis [Internet]. In: Wen PY, Eichler AF, editors. UpToDate; [updated 2024 Jun 11; cited 2024 Jan]. Available from: https://www.uptodate.com/contents/autoimmune-including-paraneoplastic-encephalitis-clinical-features-and-diagnosis?search=pediatric%20encephalitis&source=search_result&selectedTitle=1~150&usage_type=default&display_rank=1#H3369874
6. Hardy D. Autoimmune Encephalitis in Children. *Pediatr Neurol*. 2022;132:56-66. doi:10.1016/j.pediatrneurol.2022.05.004
7. Lotze TE, Chadwick DJ. Acute disseminated encephalomyelitis (ADEM) in children: Pathogenesis, clinical features, and diagnosis [Internet]. In: Patterson MC, Tung GA, Dashe JF, editors. UpToDate; [updated 2022 Oct 25; cited 2024 Jan]. Available from: https://www.uptodate.com/contents/acute-disseminated-encephalomyelitis-adem-in-children-pathogenesis-clinical-features-and-diagnosis?search=pediatric%20encephalitis&topicRef=6043&source=see_link
8. Hardarson HS, Messacar K. Acute viral encephalitis in children: Clinical manifestations and diagnosis [Internet]. In: Kaplan SL, Nordli DR, Armsby C, editors. UpToDate; [updated 2022 Dec 5; cited 2024 Jan]. Available from: https://www.uptodate.com/contents/acute-viral-encephalitis-in-children-clinical-manifestat

Developed by Emily Kacer and Dr. Brandon Meaney, McMaster University for PedsCases.com.
May 2025.

ions-and-diagnosis?search=pediatric%20encephalitis&source=search_result&selectedTitle=2~150&usage_type=default&display_rank=2#H1
9. Di Pentima C. Viral meningitis in children: Epidemiology, pathogenesis, and etiology [Internet]. In: Kaplan SL, Armsby C, editors. UpToDate; [updated 2023 Apr 3; cited 2024 Jan]. Available from: https://www.uptodate.com/contents/viral-meningitis-in-children-epidemiology-pathogenesis-and-etiology?search=pediatric%20encephalitis&topicRef=5983&source=see_link#H1
10. Kaplan SL. Bacterial meningitis in children older than one month: Clinical features and diagnosis [Internet]. In: Edwards MS, Armsby, editors. UpToDate; [updated 2023 Aug 30; cited 2024 Jan]. Available from: https://www.uptodate.com/contents/bacterial-meningitis-in-children-older-than-one-month-clinical-features-and-diagnosis?search=pediatric%20encephalitis&topicRef=5980&source=see_linkhttps://www.pedneur.com/article/S0887-8994(22)00085-6/fulltext
11. Di Pentima C. Viral meningitis in children: Clinical features and diagnosis [Internet]. In: Kaplan SL, Armsby C, editors. UpToDate; [updated 2024 Mar 29; cited 2024 Jan]. Available from: https://www.uptodate.com/contents/viral-meningitis-in-children-clinical-features-and-diagnosis?search=pediatric%20encephalitis&source=search_result&selectedTitle=9~150&usage_type=default&display_rank=9
12. Hardarson HS, Messacar K. Acute viral encephalitis in children: Treatment and prevention [Internet]. In: Edwards MS, Nordli DR, Armsby C, editors. UpToDate; [updated 2022 Dec 5; cited 2024 Jan]. Available from: https://www.uptodate.com/contents/acute-viral-encephalitis-in-children-treatment-and-prevention?search=pediatric%20encephalitis&source=search_result&selectedTitle=4~150&usage_type=default&display_rank=4#H2384584798
13. Abboud H, Titulaer MJ. Autoimmune (including paraneoplastic) encephalitis: Management [Internet]. In: Wen PY, Eichler AF, editors. UpToDate; [updated 2024 Feb 12; cited 2024 Jan]. Available from: https://www.uptodate.com/contents/autoimmune-including-paraneoplastic-encephalitis-management?search=pediatric%20encephalitis&source=search_result&selectedTitle=5~150&usage_type=default&display_rank=5