

Acute Disseminated Encephalomyelitis: A review of the epidemiology, treatments, and outcomes.

Ali, D., Cardos, B., Gorur, Y., Villalba, N. L., Janssen, N., Bartha, C., Desfontaines, P., Weerts, J., & Fajardo, P. (2019). A Rare Case of Adult Acute Disseminated Encephalomyelitis Associated with Primary Epstein-Barr Virus Infection. *European journal of case reports in internal medicine*, 6(4), 001094. [https://doi.org/10.12890/2019\\_001094](https://doi.org/10.12890/2019_001094)

Ali et al. presented a case study of a rare adult ADEM episode that was triggered by the Epstein-Barr virus. They describe the patient, including systemic and neurological symptoms that were present at time of hospitalization. They proceeded to include the treatment scheme used, and any test results that they obtained. They then linked their case study to what is already known about ADEM.

This study takes a deep look at what can be seen in an adult patient suffering from ADEM. This is helpful in that ADEM symptoms differ for each patient depending on how their lesions form. Comparing a rare case to more common knowledge helps to give a full picture of the disease in question. By understanding how ADEM presented in an adult helps to distinguish potential differences between adult and pediatric patients. This article gave information regarding potential triggers of ADEM, including parasites, which are not commonly brought up.

Ayed, H., Chaudhary, M. W., AlBaradie, R., & Mir, A. (2018). Use of Cyclophosphamide in a Child With Fulminant Acute Disseminated Encephalomyelitis. *Child neurology open*, 5, 2329048X18754631. <https://doi.org/10.1177/2329048X18754631>

This article is a case study of a three-year-old with fulminant ADEM. This article addresses possible treatment options for pediatric ADEM patients. They describe the pathology of ADEM and what immune cells it recruits for the autoimmune reaction. They also used and proposed a new treatment, cyclophosphamide, and how it worked with the patient described.

This article gave a well-organized look at a treatment scheme for pediatric ADEM, including new treatments that have not been used as frequently. They included a very thorough clinical history of the child presented, with information about his recovery after the demyelinating episode. This article allowed for better understanding of a novel treatment for pediatric ADEM that was helpful in composing a treatment list. Their description included dosage and results, along with the timeline of treatment.

Iardino, A., Garner, O., Rajasekar, S., Alexander, A., Helekar, A., Shim, G., Loveman, D., Chemitiganti, R., & Bhairavarasu, K. (2019). Atypical Presentation of Acute Disseminated Encephalomyelitis (ADEM) in a Middle-Aged Adult. *The American journal of case reports*, 20, 361–365. <https://doi.org/10.12659/AJCR.911397>

This article gave insight into the presentation and treatment of ADEM in a 46-year-old male, including images of his brain scan pre- and post-treatment. Unlike other case studies, they included the results to all the test panels, not just the

results that are unique to ADEM. They included a breakdown of ADEM from past literature.

The use of test result values is helpful in increasing the information that is available for adult ADEM patients. This helps to give a complete understanding of how the body is reacting to the demyelination event. The figures used in this article were particularly helpful in that it gave a clear visual representation of what ADEM lesions look like before and after a patient is treated with corticosteroids. This article also addressed deeper structures within the brain that can become affected by demyelination

Lademann, H., Bertsche, A., Petzold, A., Zack, F., Büttner, A., Däbritz, J., Hauenstein, C., Bahn, E., Spang, C., Reuter, D., Warnke, P., & Ehler, J. (2020). Acute Disseminated Encephalomyelitis with Seizures and Myocarditis: A Fatal Triad. *Medicina (Kaunas, Lithuania)*, 56(6), 277. <https://doi.org/10.3390/medicina56060277>

This article addresses a case study of ADEM in a pediatric female presenting with abnormal symptoms. Lademann et al. describe the hospitalization and treatment of a four-year-old presenting with ADEM, seizures, and myocarditis. They explain the treatment scheme that was utilized and its results. This triad later is found to be fatal for the child. This triad appeared to be caused by an autoimmune response not only in the brain but also in the heart.

This case study provided test results from multiple days during the child's hospitalization, which helps to provide an understanding of what changed throughout treatment. By understanding less frequent symptoms, new treatment paths can be created. This article helped to understand how frequently some

symptoms are seen in ADEM patients. It helps to expand the understanding of which viruses relate to ADEM.

Massa, S., Fracchiolla, A., Neglia, C., Argentiero, A., & Esposito, S. (2021). Update on Acute Disseminated Encephalomyelitis in Children and Adolescents. *Children (Basel, Switzerland)*, 8(4), 280. <https://doi.org/10.3390/children8040280>

Massa et al. created a comprehensive summary of information pertaining to ADEM. They included wide-ranging lists of infectious triggers, including parasites, bacteria, and viruses. Prevalence of clinical symptoms, including uncommon symptoms as tabulated to better inform the reader.

The use of figures and tables to better elaborate on ADEM helped to increase understanding of the disease. The flow chart describing a diagnostic work up outlined not only test that should be done, but what the results of those tests mean for the patient. The included meta-analysis of treatments, both common and uncommon, gives a clear path for physicians to take. This article provided valuable information on basic data and information regarding ADEM. It provided a comprehensive treatment list, including alternative treatments and dosages.

Massa et al. explored treatments that extend beyond hospitalization, including rehabilitation and supportive care that other articles did not discuss.

MedlinePlus. (2020). HLA-DRB1 gene [NIH genomic Reference]. Retrieved from

<https://medlineplus.gov/genetics/gene/hla->

[drbl/#:~:text=Type%201%20diabetes%20risk%20is,\\*02%2C%20is%20called%20DR3.](https://medlineplus.gov/genetics/gene/hla-drbl/#:~:text=Type%201%20diabetes%20risk%20is,*02%2C%20is%20called%20DR3.)

MedlinePlus defined the HLA-DRB1 gene and its ties to the immune system.

Elaborating on what aspects of the immune response that the HLA-DRB1 protein heterodimer acts on.

This provided better understanding of the genetic component of ADEM and how it works in the disease itself.

Niederschweiberer, J., Lauerer, M., Schweyer, K., Maegerlein, C., Liesche, F., Hofer, S., Berthele, A., & Lingor, P. (2020). Acute disseminated encephalomyelitis following Tdap vaccination and bacterial meningoencephalitis. *Multiple sclerosis and related disorders*, 46, 102471. <https://doi.org/10.1016/j.msard.2020.102471>

This case study reported the symptoms and treatment of an adult woman following a vaccine trigger. It addresses the timeline of CSF results following each treatment given. Included in this figure is MRIs corresponding to the days of her hospitalization. Niederschweiberer et al. include a complete description of disease progression in the patient. They address which vaccines have been associated with ADEM, including which hold greater risk in triggering a demyelinating response.

The inclusion of how the clinical symptoms presented themselves along the course of treatment allows for better understanding of how a case of ADEM may present in other patients. This case study also shed light on how adults react to demyelinating vaccine triggers that are not often seen.

Nishiyama, M., Nagase, H., Tomioka, K., Tanaka, T., Yamaguchi, H., Ishida, Y., Toyoshima, D., Fujita, K., Maruyama, A., Sasaki, K., Oyazato, Y., Nakagawa, T., Takami, Y., Nozu, K., Nishimura, N., Nakashima, I., & Iijima, K. (2019). Clinical time course of pediatric acute

disseminated encephalomyelitis. *Brain & development*, 41(6), 531–537.

<https://doi.org/10.1016/j.braindev.2019.02.011>

This article presents a retrospective clinical observation study of 24 cases of ADEM that helped to shed light on the development of ADEM and treatments that are used. They studied the characteristics of the patients that presented with ADEM, including analysis of the time course of the disease. Each time course was analyzed to better understand when each step of the disease happened, including the worsening period, the improving period, and when treatments were administered.

The data compiled helps to better understand characteristics of patients that suffer from ADEM. The data created better understanding of long-term side outcomes following a demyelinating episode. This allowed for a deeper understanding of pediatric ADEM symptoms and outcomes following certain treatment schemes.

Orbach, R., Schneebaum Sender, N., Lubetzky, R., & Fattal-Valevski, A. (2019). Increased Intracranial Pressure in Acute Disseminated Encephalomyelitis. *Journal of child neurology*, 34(2), 99–103. <https://doi.org/10.1177/0883073818811541>

This article is a retrospective cohort study that compiled data to better understand increased intracranial pressure in relation to ADEM in children. They define the clinical features for each analyzed case as well as test results pertaining to the study. They describe how increased intracranial pressure contributes to clinical signs and symptoms.

This article gives an understanding of a symptom that is usually not looked into. By connecting the differences in pressure to other results seen in patients. They address possible mechanisms for the immune response seen in ADEM patients.

Otallah S. (2021). Acute disseminated encephalomyelitis in children and adults: A focused review emphasizing new developments. *Multiple sclerosis (Houndmills, Basingstoke, England)*, 27(8), 1153–1160. <https://doi.org/10.1177/1352458520929627>

This article discusses the current view of acute disseminated encephalomyelitis (ADEM), including epidemiology, clinical presentation, pathophysiology, etc. Throughout this article, Otallah investigates the importance of myelin oligodendrocyte glycoprotein (MOG) antibodies when present in both initial and recurrent ADEM. Using MOG levels, Otallah describes potential deviations from the classical diagnosis of ADEM.

Otallah provides a comprehensive understanding of ADEM, looking at both past definitions and current treatments. He does a good job bringing in areas where future research is needed and what next steps should be in the field. This article does a great job of setting up a review of ADEM. His explanations of the disease and its treatments matches well with other articles that work to inform medical professional of an uncommon illness.

Paolilo, R. B., Deiva, K., Neuteboom, R., Rostásy, K., & Lim, M. (2020). Acute Disseminated Encephalomyelitis: Current Perspectives. *Children (Basel, Switzerland)*, 7(11), 210. <https://doi.org/10.3390/children7110210>

This article gives a view of ADEM through connecting it to acquired demyelinating syndromes along with environmental triggers. The authors focus

heavily on not only ADEM but its associated relapsing disorders, providing definitions of each one. They give in depth descriptions of all types of diagnostic testing that is used for ADEM patients and what the results mean. The authors take time to address the differences seen in adults and pediatric cases of ADEM. Paolilo et al. bring up MOG antibodies and what they mean for demyelinating disorders. Through this they provide information about future directions for research into MOG antibodies.

Paolilo et al. define recurrent forms of ADEM comprehensively to give a better understanding of the prognosis patients face. This article helps to explain treatment options for both acute phase and recurrent forms of ADEM. Each pattern of recurrence was defined using its connection to the primary ADEM episode and MOG antibodies.

Santoro, J. D., & Chitnis, T. (2019). Diagnostic Considerations in Acute Disseminated Encephalomyelitis and the Interface with MOG Antibody. *Neuropediatrics*, 50(5), 273–279. <https://doi.org/10.1055/s-0039-1693152>

This article provides diagnostic information about ADEM, specifically the IPMSSG diagnostic criteria. Using this method of diagnosis, the authors present neuroradiological images and clinical testing information to describe the criteria. Santoro et al. identify where MOG antibodies connect with current criteria as well as looking at future work that needs to be done on the subject. The authors provide a comprehensive report about differential diagnosis as it pertains to ADEM, including mimics and alternative diseases. The article addresses the



specific role that MOG antibodies play in inflammation of patients that test positive for these antibodies.

The descriptions of other neurological and genetic mimics provide a deeper understanding about the importance of differential diagnosis as it applied to ADEM. The discussion on treatment paths agrees with other articles on the subject. The author addresses the sequelae connected with ADEM by looking at their physical reasons for them.

Stadelmann, C., Timmler, S., Barrantes-Freer, A., & Simons, M. (2019). Myelin in the Central Nervous System: Structure, Function, and Pathology. *Physiological reviews*, 99(3), 1381–1431. <https://doi.org/10.1152/physrev.00031.2018>

This article addresses myelin and its importance in the central nervous system. Different pathologies related to myelin were brought up and described, including MS, ADEM, NMOSD, leukodystrophies, and mutations pertaining to myelin related genes and cells. They brought up how mutations in the cells that help myelin in the nervous system can affect the integrity of myelin in the CNS. For each myelin related pathology, they discussed causes, symptoms, and treatments. They showed how each illness differs from the others in respect to myelin. Not only did they look at pathologies related specifically to myelin, but they also looked into how changes in the cells that work along with myelin can cause damage. This gave a very well-rounded understanding of the cellular aspect of the nervous system. This article helped in creating understanding myelin and its components, especially MOG antibodies. It also described how ADEM presents in MRI images, including how lesions present and appear in patients with ADEM.

Stokes Brackett, A. C., Hernández-Fustes, O. J., Arteaga Rodríguez, C., & Hernandez Fustes, O.

J. (2020). Multiphasic acute disseminated encephalomyelitis and differential with early onset multiple sclerosis. *Intractable & rare diseases research*, 9(1), 61–63.

<https://doi.org/10.5582/irdr.2020.01009>

This article gives a better understanding of recurrent forms of ADEM as well as giving an understanding of differential diagnosis. Stokes Bracket et al.

specifically focus on neurological differential diagnosis pertaining to multiple sclerosis. Using neuroradiological findings, they compare ADEM to MS.

This article does a good job of giving criteria for physicians when performing differential diagnosis to determine treatment for their patients. They provided a good comparison between a case of ADEM and a case of MS in children looking at structural differences in the brain. Stokes Brackett et al. gave insight into how MS and ADEM differ. They also allowed for better understanding of not only the primary episode of ADEM but also of a recurrent episode as well.

Torisu, H., & Okada, K. (2019). Vaccination-associated acute disseminated encephalomyelitis. *Vaccine*, 37(8), 1126–1129.

<https://doi.org/10.1016/j.vaccine.2019.01.021>

Torisu and Okada provide an alternative diagnostic criterion that is specifically geared towards vaccination associated ADEM. The authors also completed a meta-analysis of incidence rates across the globe. They address factors that can influence vaccine associated ADEM, specifically looking at which vaccines show increased risk for each age group.

The Brighton Collaboration Encephalitis Working Group case definition added a new level of understanding of ADEM diagnosis. The provided information on the factors that influence of vaccines in regard to ADEM. The comprehensive data provided sheds light on the rare triggers of this rare disease.