***NORSE/FIRES ANNOTATED REFERENCE LIST***

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Articles are categorized as follows:

1. Terminology/Definitions/Guidelines/Consensus statements
2. Original Research
3. Systematic Reviews/Meta-analyses
4. Other Reviews
5. Case Series
6. Case Reports
7. Articles in Lay Media
8. Personal Narratives

*Within each category, articles are listed most recent first.*

*Some of the most important/highly recommended manuscripts are highlighted* ***in bold****.*

*About 130 articles are included in total.*

*The following icons, representing the type of publication or aspect of disease/science that the paper addresses, are used to label many of the references.*

Pediatrics Icon

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Etiology/Pathogenesis Icon

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Imaging A close-up of the moon

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Anesthesia Shape

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Ketogenic dietA picture containing logo

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Immunotherapy

Original ResearchA picture containing scissors, key

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Outcomes Icon

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***I. Terminology/Definitions/Guidelines/Consensus Statements***

1. **Koh, S., Wirrell, E., Vezzani, A., Nabbout, R., Muscal, E., Kaliakatsos, M., Wickström, R., Riviello, J. J., Brunklaus, A., Payne, E., Valentin, A., Wells, E., Carpenter, J. L., Lee, K., Lai, Y. C., Eschbach, K., Press, C. A., Gorman, M., Stredny, C. M., Roche, W., … Mangum, T. (2021). Proposal to optimize evaluation and treatment of Febrile infection-related epilepsy syndrome (FIRES): A Report from FIRES workshop. *Epilepsia open*, *6*(1), 62–72.** [**https://doi.org/10.1002/epi4.12447**](about:blank)

Icon

Description automatically generated *(Pediatrics)*

*An international multidisciplinary group of experts convened (FIRES workshop) to propose a protocol for the evaluation and management of pediatric FIRES. The group recommended early administration of ketogenic diet and IL-1R antagonist anakinra (that blocks biologic activity of IL-1beta), once FIRES was suspected.*

1. **Hirsch, L. J., Gaspard, N., van Baalen, A., Nabbout, R., Demeret, S., Loddenkemper, T., Navarro, V., Specchio, N., Lagae, L., Rossetti, A. O., Hocker, S., Gofton, T. E., Abend, N. S., Gilmore, E. J., Hahn, C., Khosravani, H., Rosenow, F., & Trinka, E. (2018). Proposed consensus definitions for new-onset refractory status epilepticus (NORSE), febrile infection-related epilepsy syndrome (FIRES), and related conditions. *Epilepsia*, *59*(4), 739–744. https://doi.org/10.1111/epi.14016**

*An international multidisciplinary group of experts develop proposed consensus definitions of NORSE and FIRES, and related conditions and terms.*

1. Glauser T, Shinnar S, Gloss D, Alldredge B, Arya R, Bainbridge J, Bare M, Bleck T, Dodson WE, Garrity L, Jagoda A, Lowenstein D, Pellock J, Riviello J, Sloan E, Treiman DM. Evidence-Based Guideline: Treatment of Convulsive Status Epilepticus in Children and Adults: Report of the Guideline Committee of the American Epilepsy Society. Epilepsy Curr. 2016 Jan-Feb;16(1):48-61.

*AES guideline for management of convulsive status epilepticus in adults.*

1. Nabbout R. FIRES and IHHE: Delineation of the syndromes. Epilepsia. 2013 Sep;54 Suppl 6:54–6.

Icon

Description automatically generated*(Pediatrics)*

*A short review and delineation of FIRES and IHHE (idiopathic hemiconvulsion, hemiplegia, and epilepsy syndrome)*

*(Review- 2013)*

1. Ismail FY, Kossoff EH. AERRPS, DESC, NORSE, FIRES: multi-labeling or distinct epileptic entities? Epilepsia. 2011 Nov;52(11):e185–9.

*FIRES case report and review of literature; authors suggest that AERRPS, DESC, NORSE and FIRES may be the names used for possibly the same entities.*

*(Case report-2011)*

1. Van Baalen A, Häusler M, Boor R, Rohr A, Sperner J, Kurlemann G, et al. Febrile infection-related epilepsy syndrome (FIRES): a nonencephalitic encephalopathy in childhood. Epilepsia. Blackwell Publishing Ltd; 2010 Jul;51(7):1323–8.

Icon

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Description automatically generated*(Pediatrics) (Original Research)*

*A retrospective multicenter series of 22 children with FIRES and introduction of the term FIRES.*

1. Sakuma H. Acute encephalitis with refractory, repetitive partial seizures. Brain Dev. 2009 Aug;31(7):510–4.

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1. Sakuma H, Awaya Y, Shiomi M, Yamanouchi H, Takahashi Y, Saito Y, et al. Acute encephalitis with refractory, repetitive partial seizures (AERRPS): a peculiar form of childhood encephalitis. Acta Neurol Scand. 2010 Apr;121(4):251–6.

Icon

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Description automatically generated*(Pediatrics) (Original Research)*

*Retrospective multicenter study conducted in Japan describing clinical features of a FIRES-like syndrome. The term “acute encephalitis with refractory, repetitive partial seizures” (AERRPS) was used to describe this syndrome.*

1. Mikaeloff Y, Jambaqué I, Hertz-Pannier L, Zamfirescu A, Adamsbaum C, Plouin P, et al. Devastating epileptic encephalopathy in school-aged children (DESC): a pseudo encephalitis. Epilepsy Res. 2006 Apr;69(1):67–79.

Icon

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Description automatically generated*(Pediatrics) (Original Research)*

*Description of cases of febrile illness-related epileptic encephalopathy with refractory seizures and status epilepticus in 14 children, similar or identical to FIRES, that persisted as intractable peri-sylvian epilepsy. Authors propose the term Devastating Epileptic encephalopathy in School-age Children (DESC).*

*(Case series-2006)*

1. Wilder-Smith EPV, Lim ECH, Teoh HL, Sharma VK, Tan JJH, Chan BPL, et al. The NORSE (new-onset refractory status epilepticus) syndrome: defining a disease entity. Ann Acad Med Singap. 2005 Aug;34(7):417–20.

A picture containing scissors, key

Description automatically generated*(Original Research)*

*A case series from Singapore describing 7 patients with NORSE with observations of cryptogenic prolonged status epilepticus in young women with antecedent febrile illness, CSF pleocytosis and poor outcomes. This was referred to and defined as NORSE for the first time.*

*(Case series- 2005)*

***II. Original Research***

1. Hanin A, Baudin P, Demeret S, Roussel D, Lecas S, Teyssou E, Damiano M, Luis D, Lambrecq V, Frazzini V, Decavèle M, Plu I, Bonnefont-Rousselot D, Bittar R, Lamari F, Navarro V; Study Group. Disturbances of brain cholesterol metabolism: A new excitotoxic process associated with status epilepticus. Neurobiol Dis. 2021 Jul;154:105346. doi: 10.1016/j.nbd.2021.105346. Epub 2021 Mar 24. PMID: 33774180.

A picture containing scissors, key

Description automatically generated *(Original Research)*

*A study of cholesterol homeostasis in 63 blood, 32 CSF, and 8 post-mortem brain samples from patients with status epilepticus compared to the controls showed lower 24-hydroxycholesterol in plasma followed by an increase in cholesterol synthesis. Desmosterol level was higher in CSF whereas lanosterol and dihydrolanosterol levels were higher in plasma from SE patients. The results suggested that there is brain cholesterol accumulation after status epilepticus and this could contribute to excitotoxicity.*

1. Hanin A, Demeret S, Lambrecq V, Rohaut B, Marois C, Bouguerra M, Demoule A, Beaudeux JL, Bittar R, Denis JA, Imbert-Bismut F, Lamari F, Rucheton B, Bonnefont-Rousselot D, Chavez M, Navarro V. Clinico-biological markers for the prognosis of status epilepticus in adults. J Neurol. 2022 Jun 29. doi: 10.1007/s00415-022-11199-4. Epub ahead of print. PMID: 35768546.

*A prospective cohort study of 81 patients aimed at investigating the predictors of status epilepticus severity and outcomes found that clinical markers (SE refractoriness, SE duration, and de novo SE) were significant independent predictors of clinical worsening, while lipid markers and progranulin predicted mortality better.*

1. Wu J, Lan X, Yan L, Hu Y, Hong S, Jiang L, Chen J. A retrospective study of 92 children with new-onset refractory status epilepticus. Epilepsy Behav. 2021 Nov 15; 125:108413. doi: 10.1016/j.yebeh.2021.108413. Epub ahead of print. PMID: 34794014.

Icon

Description automatically generated*(Pediatrics)*

*A retrospective study of 92 children with NORSE showed that the majority of pediatric patients with NORSE present with FIRES. The clinical features, EEG, neuroimaging and prognoses were not significantly different between the FIRES group and non-FIRES group. The presence of SRSE, diffuse cortical edema and multifocal abnormality were related to a poor prognosis.*

1. Neligan, A., Kerin, B., Walker, M. C., & Rajakulendran, S. (2021). New-Onset Refractory Status Epilepticus (NORSE): The Queen Square Neuro-ICU experience. *Epilepsy & behavior: E&B*, *125*, 108387. Advance online publication. https://doi.org/10.1016/j.yebeh.2021.108387

*In this study of 26 cases of 'NORSE', there was no difference in prognosis between 'NORSE' and non-'NORSE' RSE, nor in any sub-analysis in the 'NORSE' cohort.*

1. Chen SS, Zhang YF, Di Q, Shi JP, Wang LL, Lin XJ, et al. Predictors and prognoses of epilepsy after anti-neuronal antibody-positive autoimmune encephalitis. Seizure. 2021; 92:189-94.

Icon

Description automatically generated*(Etiology/Pathogenesis)*

*A retrospective cohort study aiming to evaluate and incidence and predictors of epilepsy after antibody positive autoimmune encephalitis concluded that although 80% patients have acute seizures, only about 40% develop epilepsy, and early initiation of immunotherapy may lower this incidence.*

1. **Sculier, C., Barcia Aguilar, C., Gaspard, N., Gaínza-Lein, M., Sánchez Fernández, I., Amengual-Gual, M., Anderson, A., Arya, R., Burrows, B.T., Brenton, J.N., Carpenter, J.L., Chapman, K.E., Clark, J., Gaillard, W.D., Glauser, T.A., Goldstein, J.L., Goodkin, H.P., Gorman, M., Lai, Y.-C., McDonough, T.L., Mikati, M.A., Nayak, A., Peariso, K., Riviello, J., Rusie, A., Sperberg, K., Stredny, C.M., Tasker, R.C., Tchapyjnikov, D., Vasquez, A., Wainwright, M.S., Wilfong, A.A., Williams, K., Loddenkemper, T. Clinical presentation of new onset refractory status epilepticus in children (the pSERG cohort) (2021) Epilepsia, 62 (7), pp. 1629-1642.**

Icon

Description automatically generated*(Pediatrics)*

*A prospective cohort study of 46 NORSE patients aiming to evaluate the significance of the relationship between fever onset and status epilepticus found that those children with onset of fever more than 24 hours prior to the onset (i.e., qualifying as FIRES) have distinctive clinical features and worse outcomes.*

1. Sheehan, T., Amengual-Gual, M., Vasquez, A., Abend, N. S., Anderson, A., Appavu, B., Arya, R., Barcia Aguilar, C., Brenton, J. N., Carpenter, J. L., Chapman, K. E., Clark, J., Farias-Moeller, R., Gaillard, W. D., Gaínza-Lein, M., Glauser, T. A., Goldstein, J. L., Goodkin, H. P., Guerriero, R. M., Huh, L., … Pediatric Status Epilepticus Research Group (2021). Benzodiazepine administration patterns before escalation to second-line medications in pediatric refractory convulsive status epilepticus. *Epilepsia*, *62*(11), 2766–2777. https://doi.org/10.1111/epi.17043

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Description automatically generated with low confidence*(Pediatrics) (Anesthesia)*

*This retrospective multicenter study from US and Canada aiming to study the benzodiazepine administration patterns in pediatric refractory convulsive status epilepticus found that failure to escalate to non-benzodiazepine ASMs occurs mainly in out-of-hospital RSE onset.*

1. Farias-Moeller, R., Wood, A., Sawdy, R., Koop, J., Olson, K., van Baalen, A. Parental perception of FIRES outcomes, emotional states, and social media usage (2021) Epilepsia Open.

Icon

Description automatically generated*(Pediatrics)*

*This survey-based study of parents of children with FIRES showed that despite their children's significantly impaired functional outcome after FIRES and high rates of medically refractory epilepsy, the cohort demonstrated remarkable emotional resilience; they perceive social media as beneficial and are interested in social media-advertised research.*

1. Yanagida, A., Kanazawa, N., Kaneko, J., Kaneko, A., Iwase, R., Suga, H., Nonoda, Y., Onozawa, Y., Kitamura, E., Nishiyama, K., Iizuka, T. Clinically based score predicting cryptogenic NORSE at the early stage of status epilepticus (2020) Neurology neuroimmunology & neuroinflammation, 7 (5).

&

1. Iizuka, T., Yanagida, A. Clinically based score predicting cryptogenic NORSE (2020) Clinical and Experimental Neuroimmunology, 11 (4), pp. 207-208.

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1. Iizuka T, Kaneko J, Kaneko A, Yanagida A, Nonoda Y, Onozawa Y, Kanazawa N, Dalmau J, Nishiyama K. A Clinically Based Score that predicts Cryptogenic New-Onset Refractory Status Epilepticus (C-NORSE). Neurology Apr 2019, 92 (15 Supplement) S11.004.

Icon

Description automatically generated*(Etiology/Pathogenesis)*

*Six clinical features (previous good health, prodromal fever, lack of psychobehavioral/memory symptoms, absence of dyskinesias and symmetric brain abnormalities) were used to create a score and patients with status epilepticus with prominent motor features and a high score were more likely to have cryptogenic NORSE.*

1. Husari, K. S., Labiner, K., Huang, R., & Said, R. R. (2020). New-Onset Refractory Status Epilepticus in Children: Etiologies, Treatments, and Outcomes. *Pediatric critical care medicine: a journal of the Society of Critical Care Medicine and the World Federation of Pediatric Intensive and Critical Care Societies*, *21*(1), 59–66. https://doi.org/10.1097/PCC.0000000000002108

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Description automatically generated*(Pediatrics) (Etiology/Pathogenesis) (Outcomes)*

*A single-center retrospective study from Texas looking at etiology, clinical presentation, therapies, and outcomes in 40 children with NORSE found that in more than half of the children the etiology remained cryptogenic and no children had neuronal antibodies detected.*

1. Matthews, E., Alkhachroum, A., Massad, N., Letchinger, R., Doyle, K., Claassen, J., Thakur, K.T. New-onset super-refractory status epilepticus: A case series of 26 patients (2020) Neurology, 95 (16), pp. e2280-e2285.

*A retrospective study of various features of the disease in 26 patients with NORSE, limited to cases with super-refractory SE, which they called “NOSRSE”. Seven patients underwent biopsy, autopsy, or both, which was diagnostic in three: herpes simplex encephalitis, candida encephalitis and acute disseminated encephalomyelitis.*

1. Rüegg, S. New-onset super-refractory status epilepticus (NOSRSE): What's in a name? (2020) Neurology, 95 (16), pp. 713-714.

*Editorial to Matthews et al NORSE study above.*

1. Gugger JJ, Husari K, Probasco JC, Cervenka MC. New-onset refractory status epilepticus: A retrospective cohort study. *Seizure*. 2020;74: 41-48. 10.1016/j.seizure.2019.12.002

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Description automatically generated*(Etiology/Pathogenesis) (Outcomes)*

*Retrospective study of a 20-patient adult cohort describing etiology, clinical features, and outcome in 20 patients with NORSE. Most were cryptogenic, with high mortality and subsequent intractable epilepsy was common.*

1. Helbig, I., Barcia, G., Pendziwiat, M., Ganesan, S., Mueller, S.H., Helbig, K.L., Vaidiswaran, P., Xian, J., Galer, P.D., Afawi, Z., Specchio, N., Kluger, G., Kuhlenbäumer, G., Appenzeller, S., Wittig, M., Kramer, U., van Baalen, A., Nabbout, R. and (2020), Whole‐exome and HLA sequencing in Febrile infection‐related epilepsy syndrome. Ann Clin Transl Neurol. doi:10.1002/acn3.51062

Icon

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Description automatically generated*(Pediatrics) (Etiology/Pathogenesis)*

*Exome sequencing in 50 individuals (29 patient-parent trios and 23 single probands) with FIRES showed no pathogenic variants in genes known to be associated with epilepsy or neurodevelopmental disorders; HLA sequencing in 29 patients did not show any allelic associations when compared against 529 population controls.*

1. Wang, D., Pan, Y., Huang, K., Lin, Z., Xie, Z., Liu, G., Wu, Y., Wang, S. Is rat hippocampus section immunostaining an indicator for immunotherapy in cryptogenic adult new-onset refractory status epilepticus (NORSE)? (2020) Seizure, 76, pp. 131-136.

Icon

Description automatically generated*(Etiology/Pathogenesis)*

*A prospective cohort study aiming to identify if immunostaining of serum/CSF is a marker of progression to SRSE and poor outcomes; they did not find significant differences between the groups with and without immunostaining.*

1. Hsieh MY, Lin JJ, Hsia SH, et al. Diminished toll-like receptor response in febrile infection-related epilepsy syndrome (FIRES). *Biomed J*. 2020;43(3):293-304. doi:10.1016/j.bj.2020.05.007

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Description automatically generated*(Pediatrics) (Etiology/Pathogenesis)*

*This study showed that children with FIRES may have impaired TLR3, TLR4, TLR7/8 and TLR9 due to either defective phagocytosis or T cell regulatory dysfunction. These were compared against children with febrile seizures and non-refractory epilepsy.*

1. Kim, HJ, Lee, S-A, Kim, H-W, Kim, SJ, Jeon, S-B, Koo, YS. The timelines of MRI findings related to outcomes in adult patients with new-onset refractory status epilepticus. *Epilepsia*. 2020; 00: 1– 14. [https://doi.org/10.1111/epi.16620](about:blank)

A close-up of the moon

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Description automatically generated*(Imaging) (Outcomes)*

*Long-term outcome of 39 patients with NORSE. Predictors of poor functional outcome and pharmacoresistant epilepsy included leptomeningeal enhancement on initial MRI and hippocampal atrophy on later MRIs.*

1. Lai, Y. C., Muscal, E., Wells, E., Shukla, N., Eschbach, K., Hyeong Lee, K., Kaliakatsos, M., Desai, N., Wickström, R., Viri, M., Freri, E., Granata, T., Nangia, S., Dilena, R., Brunklaus, A., Wainwright, M. S., Gorman, M. P., Stredny, C. M., Asiri, A., Hundallah, K., … Riviello, J. (2020). Anakinra usage in febrile infection related epilepsy syndrome: an international cohort. *Annals of clinical and translational neurology*, *7*(12), 2467–2474. https://doi.org/10.1002/acn3.51229

Icon

Description automatically generated *(Pediatrics) (Immunotherapy)*

Y

*A retrospective cohort of 25 children treated with Anakinra for FIRES. Anakinra was potentially safe with treatment discontinuation in only one child due to infection. Earlier initiation of Anakinra was associated with better outcomes.*

1. Alkhachroum A, Der-Nigoghossian CA, Mathews E, Massad N, Letchinger R, Doyle K, et al. Ketamine to treat super-refractory status epilepticus. Neurology. 2020;95(16):e2286-e94.

Shape

Description automatically generated with low confidence*(Anesthesia)*

*A retrospective multicenter study of SRSE including 68 subjects treated with ketamine showed an association with decrease in seizure burden. The data supported the notion that high dose ketamine infusion is associated with decreased vasopressor requirement without elevation in intracranial pressure.*

1. Lam, S.-K., Lu, W.-Y., Weng, W.-C., Fan, P.-C., Lee, W.-T. The short-term and long-term outcome of febrile infection-related epilepsy syndrome in children (2019) Epilepsy and Behavior, 95, pp.117-123.

Icon

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Description automatically generated*(Pediatrics) (Outcomes)*

*A retrospective study of 25 children with FIRES showed that 16% children died in hospital, most children developed refractory epilepsy and significant decline in function at hospital discharge, but there was improvement upon long term follow up.*

1. Erklauer, J., Graf, J., McPherson, M., Anderson, A., Wilfong, A., Minard, C.G., Loftis, L. Outcomes in Children Treated with Pentobarbital Infusion for Refractory and Super-Refractory Status Epilepticus (2018) Neurocritical Care, 29 (2), pp. 171-179.

Icon

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Description automatically generated*(Pediatrics) (Outcomes)*

*A retrospective cohort study of outcomes in 40 children with RSE treated with pentobarbital infusion showed 30% mortality in this group but despite prolonged pentobarbital infusion, there were cases of good neurologic outcome.*

1. Lee, H.-F., Chi, C.-S. Febrile infection-related epilepsy syndrome (FIRES): therapeutic complications, long-term neurological and neuroimaging follow-up  
   (2018) Seizure, 56, pp. 53-59.

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Description automatically generated with medium confidence *(Pediatrics) (Imaging) (Outcomes)*

*A retrospective study of 29 patients with FIRES showed that common acute complications include liver dysfunction, arrhythmias, and skin breakdown. Higher grades of periventricular white matter changes suggested poor outcome.*

1. Strohm, C. Steriade, G. Wu, S. Hantus, A. Rae-Grant and M. Larvie. FDG-PET and MRI in the Evolution of New Onset Refractory Status Epilepticus. American Journal of Neuroradiology February 2019, 40 (2) 238-244; DOI: [https://doi.org/10.3174/ajnr.A5929](about:blank)

A close-up of the moon

Description automatically generated with medium confidence *(Imaging)*

*Retrospective study of 12 patients, including 21 PET scans and 50 MRI scans during their hospitalizations showed PET abnormalities were very common and could be markers of disease activity.*

1. Clarkson, B.D.S., LaFrance‐Corey, R.G., Kahoud, R.J., Farias‐Moeller, R., Payne, E.T. and Howe, C.L. (2019), Functional deficiency in endogenous interleukin‐1 receptor antagonist in patients with febrile infection‐related epilepsy syndrome. Ann Neurol, 85: 526-537. doi:10.1002/ana.25439.

Icon

Description automatically generated*(Etiology/Pathogenesis)*

*A prospective case-control study (7 FIRES/10 controls) suggesting that FIRES is associated with reduced expression of intracellular IL-1RA isoforms and functional deficiency in IL-1RA inhibitory activity.*

1. Hocker S, Nagarajan E, Rabinstein AA, Hanson D, Britton JW. Progressive Brain Atrophy in Super- refractory Status Epilepticus. JAMA Neurol. 2016 Oct 1;73(10):1201-1207. doi: 10.1001/jamaneurol.2016.1572.

A close-up of the moon

Description automatically generated with medium confidenceIcon

Description automatically generated*(Imaging) (Outcomes)*

*In this prospective observational study, on serial imaging, brain atrophy was seen in all 19 patients with SRSE despite use of anti-seizure medications, the degree of atrophy appeared to be related to the duration of SE. There was no correlation of atrophy with clinical outcome at discharge or follow up visits.*

1. Delaj L, Novy J, Ryvlin P, Marchi NA, Rossetti AO. Refractory and super-refractory status epilepticus in adults: a 9-year cohort study. Acta Neurol Scand. 2016 Apr 15. doi: 10.1111/ane.12605.

*In this prospective swiss cohort of 804 SE (33% RSE and 4% SRSE) episodes, SRSE tended to occur in younger patients with no history of epilepsy and was associated with a high mortality.*

1. Alvarez V, Lee JW, Westover MB, Drislane FW, Novy J, Faouzi M, Marchi NA, Dworetzky BA, Rossetti AO. Therapeutic coma for status epilepticus: Differing practices in a prospective multicenter study. Neurology. 2016 Oct 18;87(16):1650-1659.

Shape

Description automatically generated with low confidence*(Anesthesia)*

*This prospective multi-center observational study aiming to compare the use of therapeutic coma between two health systems from North America vs Europe found that local practices in terms of anesthesia for RSE vary but that the use of anesthesia does not affect outcome.*

1. **Gaspard, N., Foreman, B. P., Alvarez, V., Cabrera Kang, C., Probasco, J. C., Jongeling, A. C., Meyers, E., Espinera, A., Haas, K. F., Schmitt, S. E., Gerard, E. E., Gofton, T., Kaplan, P. W., Lee, J. W., Legros, B., Szaflarski, J. P., Westover, B. M., LaRoche, S. M., Hirsch, L. J., & Critical Care EEG Monitoring Research Consortium (CCEMRC) (2015). New-onset refractory status epilepticus: Etiology, clinical features, and outcome. *Neurology*, *85*(18), 1604–1613. https://doi.org/10.1212/WNL.0000000000001940**

*Largest series (n=130) of NORSE cases via retrospective review from 13 medical centers found that 50% of cases have a possible or likely identifiable cause, mostly autoimmune or paraneoplastic encephalitis, most survivors (92%) remained on anti-seizure medications and 37% developed epilepsy.*

1. Sakuma H, Tanuma N, Kuki I, Takahashi Y, Shiomi M, Hayashi M. Intrathecal overproduction of proinflammatory cytokines and chemokines in febrile infection-related refractory status epilepticus. J Neurol Neurosurg Psychiatry 2015; 86:820-2 DOI: [10.1136/jnnp-2014-309388](about:blank)

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Description automatically generated*(Pediatrics) (Etiology/Pathogenesis)*

*This prospective case control study showed that proinflammatory cytokines (IL-6) and chemokines (IL-8/CXCL-10) were selectively upregulated in AERRPS (FIRES*). *In contrast, most T-cell-associated cytokines (IL-2, IL-17A, etc) and homoeostatic chemokines (CCL21, CXCL12, etc) remained unchanged or were downregulated. These were compared against other inflammatory neurological disorders and a group with non-inflammatory neurological disorders. The study thus provided strong suggestion towards involvement of innate immunity in pathogenesis of FIRES.*

1. Khawaja AM, DeWolfe JL, Miller DW, Szaflarski JP. New-onset refractory status epilepticus (NORSE)-- The potential role for immunotherapy. Epilepsy Behav. 2015 Jun; 47:17–23.

*(Immunotherapy)*

Y

*Retrospective study of role of immunotherapy in 11 patients with NORSE and a pooled analysis of case series from literature suggested that those receiving immunotherapy likely do better than those who do not.*

1. Petit-Pedrol M, Armangue T, Peng X, Bataller L, Cellucci T, Davis R, et al. Encephalitis with refractory seizures, status epilepticus, and antibodies to the GABAA receptor: a case series, characterisation of the antigen, and analysis of the effects of antibodies. Lancet Neurol. Elsevier; 2014 Mar;13(3):276– 86.

Icon

Description automatically generated*(Etiology/Pathogenesis)*

*Serum and CSF samples were tested in 140 patients with refractory status epilepticus with antibodies to unknown neuropil antigens. Cell based assay showed high antibody titers in serum/CSF of 6 patients. High titres of serum and CSF GABAA were found to be associated with a syndrome of severe encephalitis with seizures and refractory status epilepticus.*

1. Pugin D, Foreman B, De Marchis GM, Fernandez A, Schmidt JM, Czeisler BM, et al. Is pentobarbital safe and efficacious in the treatment of super-refractory status epilepticus: a cohort study. Crit Care. BioMed Central; 2014;18(3):R103

Shape

Description automatically generated with low confidence*(Anesthesia)*

*A retrospective study looking at outcomes after pentobarbital infusion for management of SRSE in 31 patients.*

1. Fernandez A, Lantigua H, Lesch C, Shao B, Foreman B, Schmidt JM, et al. High-dose midazolam infusion for refractory status epilepticus. Neurology. Lippincott Williams & Wilkins; 2014 Jan 28;82(4):359–65.

Shape

Description automatically generated with low confidence*(Anesthesia)*

*This retrospective case-control study of patients treated with high (median: 0.4 mg/kg/h) vs. low- dose (0.2 mg/kg/h) midazolam found that higher doses were associated with better SE control and lower mortality, despite more frequent hypotension.*

1. Jayalakshmi S, Ruikar D, Vooturi S, Alladi S, Sahu S, Kaul S, Mohandas S.

Determinants and predictors of outcome in super refractory status epilepticus--a developing country perspective. Epilepsy Res. 2014 Nov;108(9):1609-17.

Icon

Description automatically generated*(Outcomes)*

*In this retrospective cohort study of mortality of SRSE in a developing country like India showed that out of 30 SRSE patients, two-thirds of patients survived and one third had a good outcome.*

1. Gaspard N, Foreman B, Judd LM, Brenton JN, Nathan BR, McCoy BM, et al. Intravenous ketamine for the treatment of refractory status epilepticus: a retrospective multicenter study. From the Critical Care EEG Monitoring Research Consortium, editor. Epilepsia. 2013 Aug;54(8):1498–503.

Shape

Description automatically generated with low confidence*(Anesthesia)*

*A multicenter retrospective study of ketamine use in 58 instances of refractory status epilepticus that showed that ketamine was safe and relatively effective in the management.*

1. Höftberger R, Titulaer MJ, Sabater L, Dome B, Rózsás A, Hegedus B, et al. Encephalitis and GABAB receptor antibodies: novel findings in a new case series of 20 patients. Neurology. Lippincott Williams & Wilkins; 2013 Oct 22;81(17):1500–6.

Icon

Description automatically generated*(Etiology/Pathogenesis)*

*A 20-patient series describing the clinical phenotype of GABAB R Ab to include limbic encephalitis, ataxia, opsoclonus-myoclonus syndrome and status epilepticus. These were observed to usually respond to treatment although the long-term prognosis is determined by presence of a tumor.*

1. Kilbride RD, Reynolds AS, Szaflarski JP, Hirsch LJ. Clinical Outcomes Following Prolonged Refractory Status Epilepticus (PRSE). Neurocrit Care. 2013 Mar 12;18(3):374–85.

Icon

Description automatically generated*(Outcomes)*

*This retrospective study of 63 subjects found that good outcome was still possible despite prolonged therapeutic coma (at times for months) for prolonged, super-refractory SE that was defined as SE persisting despite one week of induced coma.*

1. Appenzeller S, Helbig I, Stephani U, Hausler M, Kluger G, Bungeroth M, et al. Febrile infection-related epilepsy syndrome (FIRES) is not caused by SCN1A, POLG, PCDH19 mutations or rare copy number variations. Dev Med Child Neurol. 2012;54(12):1144-8.

Icon

Description automatically generatedIcon

Description automatically generated*(Pediatrics) (Etiology/Pathogenesis)*

*Despite phenotypic similarities with certain genetic epilepsies, extensive genetic analysis for the candidate genes PCDH19, SCN1A or POLG mutations was unrevealing.*

1. Kramer U, Chi C-S, Lin K-L, Specchio N, Sahin M, Olson H, et al. Febrile infection-related epilepsy syndrome (FIRES): pathogenesis, treatment, and outcome: a multicenter study on 77 children. Epilepsia. 2011 Nov;52(11):1956–65.

Icon

Description automatically generated*(Pediatrics)*

*Retrospective multicenter study of 77 children with NORSE found that no therapeutic agent was efficacious in shortening the acute phase, with the possible exception of a ketogenic diet.*

1. Rossetti AO, Milligan TA, Vulliémoz S, Michaelides C, Bertschi M, Lee JW. A randomized trial for the treatment of refractory status epilepticus. Neurocrit Care. 2011 Feb;14(1):4–10.

Shape

Description automatically generated with low confidence*(Anesthesia)*  
*This randomized controlled trial compared propofol and barbiturates for the treatment of refractory SE. It was aborted due to low enrollment rate. Efficacy of the two drugs was similar but barbiturates were associated with a longer intubation time*

***III. Systematic Reviews/Meta-analyses***

1. Lattanzi S, Leitinger M, Rocchi C, Salvemini S, Matricardi S, Brigo F, Meletti S, Trinka E. Unraveling the enigma of new-onset refractory status epilepticus: a systematic review of aetiologies. Eur J Neurol. 2022 Feb;29(2):626-647. doi: 10.1111/ene.15149. Epub 2021 Nov 2. PMID: 34661330.

*A systematic review of etiology of NORSE that showed that about half the cases are cryptogenic; of the identified causes, autoimmune encephalitis is the most common in adults and infections in children.*

1. Dozieres-Puyravel B, Hohn S, Auvin S. Considering safety and patient tolerance in the use of ketogenic diet in the management of refractory and super-refractory status epilepticus: a systematic review. Expert Rev Neurother. 2021;21(11):1303-8.

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Description automatically generated*(Ketogenic diet)*

*A systematic review of efficacy and safety of ketogenic diet in refractory and super-refractory status epilepticus. The diet was found to be effective and side effects mild.*

1. Natasha E. Schoeler, Zoe Simpson, Runming Zhou, Suresh Pujar, Christin Eltze, J. H. Cross, Dietary Management of Children With Super-Refractory Status Epilepticus: A Systematic Review and Experience in a Single UK Tertiary Centre, Frontiers in Neurology, 10.3389/fneur.2021.643105, 12, (2021).

Icon

Description automatically generatedA picture containing logo

Description automatically generated*(Pediatrics) (Ketogenic diet)*

*An eight-patient series and systematic literature review of ketogenic diet treatment (KDT) for management of SRSE suggested that KDT is feasible and safe and early initiation has the potential for efficacy in about two thirds of patients with SRSE.*

1. Specchio, N., Pietrafusa, N. New-onset refractory status epilepticus and febrile infection-related epilepsy syndrome (2020) Developmental Medicine and Child Neurology, 62 (8), pp. 897-905.

*A systematic review of all NORSE and FIRES cases published between 2003-2019 summarizing the clinical neurophysiological, imaging, treatment, and outcome data. This study showed that 70% of adult NORSE have abnormal MRI at presentation while 61% of pediatric FIRES had normal MRI at presentation.*

1. Kessi M, Liu F, Zhan Y, et al. Efficacy of different treatment modalities for acute and chronic phases of the febrile infection-related epilepsy syndrome: A systematic review. *Seizure*. 2020;79:61-68. doi:10.1016/j.seizure.2020.04.015.

A picture containing logo

Description automatically generated*(Ketogenic diet)*

*In this systematic review of literature of FIRES treatments and outcomes that had most patients from Asian countries, a positive outcome had an association with use of ketogenic diet.*

1. Ferlisi M, Shorvon S. The outcome of therapies in refractory and super-refractory convulsive status epilepticus and recommendations for therapy. Brain. Oxford University Press; 2012 Aug;135(Pt 8):2314–28.

Shape

Description automatically generated with low confidence*(Anesthesia)*

*Authors conduct as systematic review of various anesthetic treatments for refractory and super-refractory status epilepticus. The study includes limited outcome assessments for each of the therapies included. They define the entity of super-refractory SE make broad recommendations regarding optimal therapy.*

1. Tan RYL, Neligan A, Shorvon SD. The uncommon causes of status epilepticus: a systematic review. Epilepsy Res. Elsevier; 2010 Oct;91(2-3):111–22.

Icon

Description automatically generated*(Etiology/Pathogenesis)*

*This review of literature from 1990-2008 found more than 180 unusual causes of status epilepticus. They could be organized into four main categories: inflammatory, infectious, genetic, and toxic or drug-related*

***IV. Other Reviews***

1. Trinka E, Leitinger M. Management of Status Epilepticus, Refractory Status Epilepticus, and Super-refractory Status Epilepticus. Continuum (Minneap Minn). 2022 Apr 1;28(2):559-602. doi: 10.1212/CON.0000000000001103. PMID: 35393970.

*A comprehensive review of definitions, concepts, epidemiology, etiology, and management of status epilepticus, including a discussion of NORSE*

1. Périn B, Szurhaj W. New-onset refractory status epilepticus: State of the art. Rev Neurol (Paris). 2022 Jan-Feb;178(1-2):74-83. doi: 10.1016/j.neurol.2021.12.005. Epub 2022 Jan 12. PMID: 35031143.

*A review of clinical features of NORSE/FIRES.*

1. Stavropoulos I, Pak HL, Valentin A. Neuromodulation in Super-refractory Status Epilepticus. J Clin Neurophysiol. 2021 Nov 1;38(6):494-502. doi: 10.1097/WNP.0000000000000710. PMID: 34261110.

*The authors discuss the neuromodulation techniques for controlling super-refractory SE when conventional treatments have failed. These include electroconvulsive therapy, vagus nerve stimulation, transcranial magnetic stimulation, and deep brain stimulation.*

1. Mantoan Ritter, L., Nashef, L. New-onset refractory status epilepticus (NORSE) (2021) Practical Neurology, 21 (2), art. no. 002534, pp. 119-127.

*A comprehensive review of current literature on NORSE/FIRES that includes a flow diagram for evaluation and management of NORSE/FIRES (reproduced from NORSE institute).*

1. Tan TH, Perucca P, O'Brien TJ, Kwan P, Monif M. Inflammation, ictogenesis, and epileptogenesis: An exploration through human disease. *Epilepsia*. 2021;62(2):303-324. doi:10.1111/epi.16788.

Icon

Description automatically generated*(Etiology/Pathogenesis)*

*A review discussing the role of different components of immune system in various types of acute seizures and epilepsy including NORSE/FIRES.*

1. Lin, W.-S., Hsu, T.-R. Hypothesis: Febrile infection-related epilepsy syndrome is a microglial NLRP3 inflammasome/IL-1 axis-driven autoinflammatory syndrome  
   (2021) Clinical and Translational Immunology, 10 (6), art. no. e1299.

Icon

Description automatically generated*(Etiology/Pathogenesis)*

*By a review of literature authors here hypothesize that of overactivation of microglial NLRP3 inflammasome/interleukin-1 axis is the driving event in FIRES by creating a proinflammatory and proconvulsive milieu.*

1. Kirmani, B.F., Au, K., Ayari, L., John, M., Shetty, P., Delorenzo, R.J. Super-refractory status epilepticus: Prognosis and recent advances in management (2021) Aging and Disease, 12 (4), pp. 1097-1119.

Shape

Description automatically generated with low confidence*(Anesthesia)*

*A comprehensive review of various treatment options for SRSE.*

1. Yamanaka G, Ishida Y, Kanou K, et al. Towards a Treatment for Neuroinflammation in Epilepsy: Interleukin-1 Receptor Antagonist, Anakinra, as a Potential Treatment in Intractable Epilepsy. *Int J Mol Sci*. 2021;22(12):6282. Published 2021 Jun 11. doi:10.3390/ijms22126282.

Icon

Description automatically generated *(Pediatrics) (Immunotherapy)*

Y

*A review of literature on anakinra use in children with FIRES and drug resistant epilepsy showed marked improvement in some patients with FIRES and most patients with drug resistant epilepsy.*

1. Katz JB, Owusu K, Nussbaum I, Beekman R, DeFilippo NA, Gilmore EJ, et al. Pearls and Pitfalls of Introducing Ketogenic Diet in Adult Status Epilepticus: A Practical Guide for the Intensivist. J Clin Med. 2021;10(4).

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Description automatically generated*(Ketogenic diet)*

*A case report with review of literature discussing the feasibility and practical issues of use of ketogenic diet for status epilepticus.*

1. Kazazian K, Kellogg M, Wong N, et al. How to Help Your Patients Enroll in the New-Onset Refractory Status Epilepticus (NORSE) and Febrile Infection-Related Epilepsy Syndrome (FIRES) Family Registry, and Other Rare Epilepsy Registries [published online ahead of print, 2021 Mar 26]. *Epilepsy Curr*. 2021;15357597211002869. doi:10.1177/15357597211002869

*Paper informing health care providers of the NORSE/FIRES family registry created by the NORSE institute. Patients or their medical team anywhere in the world can directly enter their data into the registry and continue to enter long term data.*

1. Lee, Y.-J. Febrile infection-related epilepsy syndrome: Refractory status epilepticus and management strategies. (2020) Annals of Child Neurology, 28 (1), pp. 8-15.

*A review of clinical features, terminology, diagnostic challenges, therapeutic options for FIRES.*

1. Payne ET, Koh S, Wirrell EC. Extinguishing Febrile Infection-Related Epilepsy Syndrome: Pipe Dream or Reality? Semin Neurol. 2020;40(02):263-272. doi:10.1055/s-0040-1708503.

*A review of NORSE/ FIRES*

1. Sakuma, H., Horino, A., Kuki, I. Neurocritical care and target immunotherapy for febrile infection-related epilepsy syndrome (2020) Biomedical Journal, 43 (3), pp. 205-210.

*A review of NORSE/FIRES management.*

1. Hanin A, Lambrecq V, Denis JA, Imbert-Bismut F, Rucheton B, Lamari F, Bonnefont-Rousselot D, Demeret S, Navarro V. Cerebrospinal fluid and blood biomarkers of status epilepticus. Epilepsia. 2020 Jan;61(1):6-18. doi: 10.1111/epi.16405. Epub 2019 Dec 11. PMID: 31828792.

Icon

Description automatically generated*(Outcomes)*

*Specific protein markers can be detected in blood and CSF that serve as an evidence of neuronal injury from status epilepticus. These include neuron specific enolase, S100-beta, high mobility group box 1, and progranulin. These may have a role in prediction of severity of disability and subsequent epilepsy.The authors summarize the findings from studies involving patients and animal models of status epilepticus.*

1. Sculier, C., Gaspard, N. New onset refractory status epilepticus (NORSE) (2019) Seizure, 68, pp.72-78

*Narrative review summarizing clinical features, suggested evaluation, treatment and prognosis in NORSE/FIRES.*

1. Serino, D., Santarone, M.E., Caputo, D., Fusco, L. Febrile infection-related epilepsy syndrome (FIRES): Prevalence, impact and management strategies (2019) Neuropsychiatric Disease and Treatment, 15, pp. 1897-1903.

*A review of all aspects of FIRES as stated for the review above.*

1. Gofton, T.E., Gaspard, N., Hocker, S.E., Loddenkemper, T., Hirsch, L.J. New onset refractory status epilepticus research: What is on the horizon? (2019) Neurology, 92 (17), pp. 802-810

*A narrative review of NORSE/FIRES and a call for multi-center international collaboration, proposal of future research directions.*

*(Future directions/research initiates)*

1. Gaspard, N., Hirsch, L. J., Sculier, C., Loddenkemper, T., van Baalen, A., Lancrenon, J., Emmery, M., Specchio, N., Farias-Moeller, R., Wong, N., & Nabbout, R. (2018). New-onset refractory status epilepticus (NORSE) and febrile infection-related epilepsy syndrome (FIRES): State of the art and perspectives. *Epilepsia*, *59*(4), 745–752. https://doi.org/10.1111/epi.14022

*A review article published in Jan 2018, where nine experts discuss the proceedings of the first international NORSE/FIRES symposium that include consensus definitions, pathophysiology, possible biomarkers, therapies, and future directions of research.*

1. Josep Dalmau, Francesc Graus. Antibody Mediated Encephalitis. N Engl J Med 2018; 378:840-851. DOI: 10.1056/NEJMra1708712.

Icon

Description automatically generated*(Etiology/Pathogenesis)*

*A narrative review* *discussing various antibodies as a cause of encephalitis and their varied clinical and radiological presentations.*

1. Nabbout R, Vezzani A, Dulac O, Chiron C. Acute encephalopathy with inflammation-mediated status epilepticus. Lancet Neurol. 2011 Jan;10(1):99–108.

Icon

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Description automatically generated*(Pediatrics) (Etiology/Pathogenesis)*

*Narrative review of literature to support authors’ view that FIRES and IHHS are conditions where the status epilepticus is mediated by inflammation.*

1. Shorvon S, Ferlisi M. The treatment of super-refractory status epilepticus: a critical review of available therapies and a clinical treatment protocol. Brain. Oxford University Press; 2011 Oct;134(Pt 10):2802–18.

Shape

Description automatically generated with low confidence*(Anesthesia)*

*A review of potential therapies and suggestion of a protocol/flowchart for management of SRSE.*

***V. Case series***

1. Manganotti P, Furlanis G, Ajčević M, Moras C, Bonzi L, Pesavento V, Buoite Stella A. Intravenous immunoglobulin response in new-onset refractory status epilepticus (NORSE) COVID-19 adult patients. J Neurol. 2021 Oct;268(10):3569-3573. doi: 10.1007/s00415-021-10468-y. Epub 2021 Mar 11. PMID: 33709220; PMCID: PMC7951121.

*Two patients with NORSE (onset at admission in one and after day 11 in the other) in the setting of COVID-19 with good response to IVIG.*

1. Suchdev K, Kupsky WJ, Mittal S, Shah AK. Histopathology of new-onset refractory status epilepticus (NORSE) in adults. Seizure. 2021; 93:95-101.

Icon

Description automatically generated*(Etiology/Pathogenesis)*

*A 5-patient case series describing the histopathological findings in adults with NORSE.*

1. Nass RD, Taube J, Bauer T, Rüber T, Surges R, Helmstaedter C. Permanent loss of independence in adult febrile-infection-related epilepsy syndrome survivors: an underestimated and unsolved challenge. Eur J Neurol. 2021 Sep;28(9):3061-3071. doi: 10.1111/ene.14958. Epub 2021 Jul 2. PMID: 34091969.

Icon

Description automatically generated*(Outcomes)*

*Long term follow up of six FIRES patients suggesting survivors experience a significant loss of functional independence due to seizures, cognitive dysfunction.*

1. Horino, A., Kuki, I., Inoue, T., Nukui, M., Okazaki, S., Kawawaki, H., Togawa, M., Amo, K., Ishikawa, J., Ujiro, A., Shiomi, M., & Sakuma, H. (2021). Intrathecal dexamethasone therapy for febrile infection-related epilepsy syndrome. *Annals of clinical and translational neurology*, *8*(3), 645–655. https://doi.org/10.1002/acn3.51308

Icon

Description automatically generated *(Pediatrics) (Immunotherapy)*

Y

*In this series of six children treated with intrathecal dexamethasone (ITD) for FIRES, it was observed that ITD could shorten the critical stage of the disease. There was a significant reduction in select CSF cytokines/chemokines (such as CXCL-10, neopterin) following treatment but not all (such as IL-6, IL-8, IL-1beta) that were elevated prior to ITD (compared to epilepsy patients as controls).*

1. Manganotti, P., Furlanis, G., Ajčević, M., Moras, C., Bonzi, L., Pesavento, V., Buoite Stella, A. Intravenous immunoglobulin response in new-onset refractory status epilepticus (NORSE) COVID-19 adult patients (2021) Journal of Neurology.

Y

*(Immunotherapy)*

*A report of 2 patients with COVID-associated NORSE managed with IVIG.*

1. Lim GY, Chen CL, Chan Wei Shih D. [Utility and Safety of Perampanel in Pediatric FIRES and Other Drug-Resistant Epilepsies.](https://nam04.safelinks.protection.outlook.com/?url=https%3A%2F%2Fpubmed.ncbi.nlm.nih.gov%2F34820471%2F&data=04%7C01%7Czubeda.sheikh%40hsc.wvu.edu%7C15b78616496d4d45ec8208d9b41c07ac%7Ca2d1f95f851044248ae15c596bdbd578%7C0%7C0%7C637738854754402792%7CUnknown%7CTWFpbGZsb3d8eyJWIjoiMC4wLjAwMDAiLCJQIjoiV2luMzIiLCJBTiI6Ik1haWwiLCJXVCI6Mn0%3D%7C3000&sdata=kFAp82wMccTVWpnB3GtJieXShpY6VLqQSs%2Fn3F6Va0k%3D&reserved=0) Child Neurol Open. 2021 Nov 20; 8:2329048X211055335. doi: 10.1177/2329048X211055335. eCollection 2021 Jan-Dec. PMID: 34820471.

Icon

Description automatically generated*(Pediatrics)*

*A retrospective observational study of perampanel in 20 patients with drug resistant epilepsy and FIRES, where perampanel was used for three children with FIRES and seizures stopped within a day on days 19 and 32 of hospitalization.*

1. Wang, X., Gao, X., Lu, G., Lu, Z., Zhou, S., Wang, Y., & Zhou, Y. (2020). The ketogenic diet for paediatric patients with super-refractory status epilepticus in febrile infection-related epilepsy syndrome. Acta Epileptologica, 2(1), 4. [https://doi.org/10.1186/s42494-020-00013-1](about:blank)

Icon

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Description automatically generated*(Pediatrics) (Ketogenic diet)*

*This 7-patient series studied the efficacy of ketogenic diet in 10 pediatric patients presenting with FIRES. All 10 patients achieved ketosis in 24-72 hours. SE was controlled in 8 patients within 2-19 days of initiation of KD, one had serious adverse effects (V.fib).*

1. Aurangzeb, S., Prisco, L., Adcock, J., Speirs, M., Raby, S., Westbrook, J., Sen, A. New-onset super refractory status epilepticus: A case-series (2020) Seizure, 75, pp. 174-184.

*A 7-patient retrospective case series of NORSE describing the etiology, clinical and EEG characteristics, treatment response and outcomes.*

1. Deshmukh, N., Singh, R., Lalla, R., Karapurkar, A., Khadilkar, S. Rare complication of carotid stenting: New-onset refractory status epilepticus: A study of five patients (2019) Annals of Indian Academy of Neurology, 22 (2), pp. 210-212.

Icon

Description automatically generated*(Etiology/Pathogenesis)*

1. Choi, J.Y., Kim, E.J., Moon, S.Y., Kim, T.-J., Huh, K. Prognostic significance of subsequent extra-temporal involvement in cryptogenic new onset refractory status epilepticus (NORSE) initially diagnosed with limbic encephalitis (2019) Epilepsy Research, 158, art. no. 106215,

A close-up of the moon

Description automatically generated with medium confidence *(Imaging)*

*A 13-patient series of NORSE with limbic encephalitis observed that on follow up imaging 10/13 had extra-temporal lesion extension, most commonly to claustrum. Lesion extension was associated with poor outcome.*

1. Kim, D.-H., Yang, T.-W., Kwon, O.-Y., Kim, Y.-S. Early immunotherapy in cryptogenic new onset refractory status epilepticus (NORSE), a case series (2019) Neurology Asia, 24 (1), pp. 61-65.

*(Immunotherapy)*

Y

*A two-patient series with an observation of good outcomes with early immunotherapy (steroids, IVIG and plasmapheresis).*

1. Jun JS, Lee ST, Kim R, Chu K, Lee SK. Tocilizumab treatment for new onset refractory status epilepticus. Ann Neurol. 2018;84(6):940-5.

Y

*Experience with* *tocilizumab in 7 NORSE patients who were refractory to conventional immune therapy. Good response was reported in 6/7.*

1. Gaspard, N. A New Hose to Extinguish the FIRES? (2019) Epilepsy Currents, 19 (2), pp. 86-87.

*Editorial for the tocilizumab paper above.*

1. Thakur, K. T., Probasco, J. C., Hocker, S. E., Roehl, K., Henry, B., Kossoff, E. H., Kaplan, P. W., Geocadin, R. G., Hartman, A. L., Venkatesan, A., & Cervenka, M. C. (2014). Ketogenic diet for adults in super-refractory status epilepticus. *Neurology*, *82*(8), 665–670. <https://doi.org/10.1212/WNL.0000000000000151>.

Icon

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Description automatically generated*(Pediatrics) (Ketogenic diet)*

*Retrospective multicenter case series of 10 patients managed for SRSE with ketogenic diet.*

1. Gall CRE, Jumma O, Mohanraj R. Five cases of new onset refractory status epilepticus (NORSE) syndrome: outcomes with early immunotherapy. Seizure. 2013 Apr;22(3):217–20.

*(Immunotherapy)*

Y

*A 5-patient series with an observation of good outcome with early immunotherapy (steroids and IVIG).*

1. Holzer, F. J., Rossetti, A. O., Heritier-Barras, A. C., Zumsteg, D., Roebling, R., Huber, R., Lerche, H., Kiphuth, I. C., Bardutzky, J., Bien, C. G., Tröger, M., Schoch, G., Prüss, H., & Seeck, M. (2012). Antibody-mediated status epilepticus: a retrospective multicenter survey. European neurology, 68(5), 310–317. https://doi.org/10.1159/000341143

Icon

Description automatically generated*(Etiology/Pathogenesis)*

*A 13-patient European series of antibody mediated status epilepticus observed that this condition was severe but potentially reversible and long duration did not necessarily imply fatal outcome.*

1. Li J, Saldivar C, Maganti RK. Plasma exchange in cryptogenic new onset refractory status epilepticus. Seizure. 2012 Oct 12;22(1):70–3.

*(Immunotherapy)*

Y

*A three-patient series of experience with plasma exchange in cryptogenic NORSE.*

1. Van Lierde I, Van Paesschen W, Dupont P, Maes A, Sciot R. De novo cryptogenic refractory multifocal febrile status epilepticus in the young adult: a review of six cases. Acta Neurol Belg. 2003 Jun;103(2):88–94.

*One of the early case series (2003) describing the clinical course of six adults with NORSE/FIRES.*

1. Costello DJ, Kilbride RD, Cole AJ. Cryptogenic New Onset Refractory Status Epilepticus (NORSE) in adults-Infectious or not? J Neurol Sci. 2009 Feb 15;277(1-2):26–31.

Icon

Description automatically generated*(Etiology/Pathogenesis)*

*In this 6-patient series, authors propose that the etiology of NORSE is likely heterogeneous, with a proportion being non-infectious. The paper includes the first detailed list of tests that should be performed to identify a potential cause.*

***VI. Case reports***

1. Nawfal O, Toufaili H, Dib G, Dirani M, Beydoun A. New-onset refractory status epilepticus as an early manifestation of multisystem inflammatory syndrome in adults after COVID-19. Epilepsia. 2022 May;63(5):e51-e56. doi: 10.1111/epi.17231. Epub 2022 Mar 27. PMID: 35306658; PMCID: PMC9111422.
2. Acampora R, Quiroga Subirana P, Durante L, Tonziello R, Aversano G, Lieto M, Ripa P, Mazzaferro MP. A case of febrile infection-related epilepsy syndrome (FIRES) in young adult: still a diagnostic and therapeutic challenge. Neurol Sci. 2022 May 4:1–4. doi: 10.1007/s10072-022-06106-8. Epub ahead of print. PMID: 35507191; PMCID: PMC9064715.
3. Ruiz-Gaviria R, Ruiz-Gaviria R, Villarin LG, Villarin LG, Ross R, Ross R, Janani C, Janani C. Neurosyphilis presenting as new onset refractory status epilepticus: one of the multifarious faces of a great imitator. Sex Health. 2022 Apr 28. doi: 10.1071/SH21190. Epub ahead of print. PMID: 35477505.
4. Marx B, Hafid K, Henry P, Ledoux D, Bodart O. New onset refractory status epilepticus and neuroendocrine tumour: a case report and review of the literature. Acta Neurol Belg. 2022 Feb 12. doi: 10.1007/s13760-022-01886-4. Epub ahead of print. PMID: 35150438.
5. Juneja P, Swor D. An Evidence-Based Approach to Diagnosis and Prognosis in a Young Woman with New-Onset Super-Refractory Status Epilepticus: A Case Report. Case Rep Neurol. 2022 Jan 17;14(1):5-11. doi: 10.1159/000519947. PMID: 35221970; PMCID: PMC8832188.
6. Dono F, Carrarini C, Russo M, De Angelis MV, Anzellotti F, Onofrj M, Bonanni L. New-onset refractory status epilepticus (NORSE) in post SARS-CoV-2 autoimmune encephalitis: a case report. Neurol Sci. 2021 Jan;42(1):35-38. doi: 10.1007/s10072-020-04846-z. Epub 2020 Nov 3. PMID: 33145624; PMCID: PMC7608104.
7. Aladdin Y, Shirah B. New-onset refractory status epilepticus following the ChAdOx1 nCoV-19 vaccine. J Neuroimmunol. 2021 Aug 15;357:577629. doi: 10.1016/j.jneuroim.2021.577629. Epub 2021 Jun 7. PMID: 34153802; PMCID: PMC8182981.
8. Wadayama T, Shimizu M, Yata T, Ishikura T, Kajiyama Y, Hirozawa D, Okuno T, Mochizuki H. Cryptogenic new-onset refractory status epilepticus responded to anti-interleukin-6 treatment. J Neuroimmunol. 2022 Feb 15;363:577789. doi: 10.1016/j.jneuroim.2021.577789. Epub 2021 Dec 15. PMID: 34973472.
9. Orlandi N, Giovannini G, Mirandola L, Monti G, Marudi A, Mosca F, Lalla A, d'Orsi G, Francavilla M, Meletti S. An ultra-long new onset refractory status epilepticus: Winning the battle but losing the war? Epilepsy Behav Rep. 2022 Mar 24;18:100537. doi: 10.1016/j.ebr.2022.100537. PMID: 35445189; PMCID: PMC9014360.
10. Palacios-Mendoza M, Gómez A, Prieto J, Barrios JC, Orera M, Massot-Tarrús A. Response to anakinra in new-onset refractory status epilepticus: A clinical case. Seizure. 2022 Jan;94:92-94. doi: 10.1016/j.seizure.2021.11.014. Epub 2021 Dec 4. PMID: 34875544.
11. Al-Chalabi M, Amsdell J, Iftikhar S, Hollingshead C, Rashid M, Sheikh A. New onset refractory status epilepticus secondary to HIV CNS viral escape syndrome: Case report. Seizure. 2022 Jan;94:112-114. doi: 10.1016/j.seizure.2021.11.027. Epub 2021 Dec 4. Erratum in: Seizure. 2022 Feb;95:90. PMID: 34894438.
12. Aydemir S, Kandula P. High dose cannabidiol (CBD) in the treatment of new-onset refractory status epilepticus (NORSE). Seizure. 2022 Jan;94:126-128. doi: 10.1016/j.seizure.2021.11.020. Epub 2021 Nov 26. PMID: 34896815.
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***VIII Personal Narrative***

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