THE LANCET

Supplementary appendix

This appendix formed part of the original submission and has been peer reviewed. We post it as supplied by the authors.

Supplement to: Murphy OC, Messacar K, Benson L, et al. Acute flaccid myelitis: cause, diagnosis, and management. *Lancet* 2020; published online Dec 21. http://dx.doi.org/10.1016/S0140-6736(20)32723-9.

Supplementary Appendix to:

Murphy OC, Messacar K, Benson L, et. al.

Acute Flaccid Myelitis: Etiology, diagnosis and management

Table of Contents

Supplemental Recommendations

A. Supplemental Recommendations for Intensive Care Management of Acute Flaccid Myelitis

Critical Care and Intensive Care Unit Subgroup of the Acute Flaccid Myelitis Working Group
Jessica Carpenter[1], Elizabeth Wells[1], Raquel Farias-Moeller[2], Jay Desai[3], Caitlin O'Brien[4], Jennifer Rice[4], Melania Bembea[4], Rebecca Riggs[4], Meghan Moore[4], Amy Bayliss[4]
[1] Children's National Health System, Department of Neurology, Washington, DC
[2] Children's Hospital of Wisconsin and the Medical College of Wisconsin, Department of Neurology, Milwaukee, WI, USA.
[3] Children's Hospital Los Angeles, Division of Neurology, Los Angeles, CA, USA.
[4] Johns Hopkins University School of Medicine, Departments of Anesthesiology and Critical Care Medicine (C.O.B, M.B., R.R.), Pediatrics (J.R.), and Physical Medicine and Rehabilitation (M.M., A.B.), Baltimore, MD, USA.

I. Respiratory failure:

Patients with AFM are at high risk for respiratory failure. Supportive care can be structured to minimize the risk for intubation and prolonged ICU admission. The cause for respiratory failure in most cases is hypoventilation secondary to weakness. Patients may also have bulbar weakness and thus be at risk for aspiration.

1. Monitoring for respiratory insufficiency and/or failure

a) Identify high risk patients: poor head control, drooling, inability to raise arms above the head.
b) Education: principles of respiratory failure due to neuromuscular weakness should be reviewed across disciplines, including bedside nurses and RT.
c) Measurements:
    i. Patients age ≥ 6 years should be monitored with Q 4 hour NIFs and FVC Q 4 hours while awake (schedule can be liberalized to Q 6 while asleep).
    ii. Patients < 6 years may be able to participate in singing a song or humming on a single breath. Performance on a single task can be documented and repeated multiple times per day.

2. Supportive measures to minimize the risk for respiratory failure

a) Early mobilization (consult PT/OT and PM&R at time of diagnosis for assessment)
b) Chest PT, inhaled medications and mucolytics as indicated
c) Cough assist
d) Aggressive screening for infection and treatment where appropriate
e) Minimize sedation (see below for expanded discussion).
f) Avoidance of medications that may make exacerbate weakness (e.g. magnesium, paralytics, steroids, opioids, etc)
g) Promotion of sleep and maintenance of day night cycles
h) Formal swallowing evaluation recommended prior to initiation of oral diet to assess for aspiration risk
i) Psychology and/or Child Life consult early on may assist with anxiety and behavioral challenges

3. Sedation

a) Institutional sedation protocols should be reviewed for potential to increase the risk for respiratory failure.
b) Sedated procedures: Advanced planning is recommended.
    i. Sedating team (critical care or anesthesia) should be alerted to risk for respiratory failure so they can plan to provide medications with low risk for respiratory suppression (e.g. dexmedetomidine, ketamine, propofol).
    ii. Short acting agents are preferred when opioids and benzodiazepines must be provided (e.g. fentanyl > hydromorphone and midazolam > diazepam) .
    iii. Procedures should be modified where appropriate to minimize the exposure to sedation.
    iv. Environmental modifications can be optimized to reduce the need for sedation (e.g. Child Life involvement, allowing parents to be present in the MRI suite, explaining procedures to the child prior to initiation).
c) Sedation while intubated
    i. Medications with decreased effect on respiration are preferred (e.g. dexmedetomidine).

ii. Patients may benefit from non-infusion medications to decrease exposure to narcotics and benzodiazepines (e.g. clonidine, gabapentin).

4. Criteria for respiratory failure and threshold for implementing mechanical ventilation into the care plan.

a) The threshold for intubation should be similar to parameters for other acute neuromuscular disorders (such as Guillan-Barre Syndrome and Myasthenia Gravis)
   i. Vital capacity ≤20 mL/kg
   ii. NIF less than -30 cmH_2O
   iii. $PaCO_2$ to ≥50 mmHg
   iv. Desaturation and/or O2 requirement
   v. Sweating about the head and neck, wide pulse pressure, tachypnea, tachycardia; may reflect CO_2 retention
b) Patients with inability to swallow or manage secretions may also benefit from intubation.
c) Considered nasal intubation for younger patients (less noxious and tolerated with less sedation).
d) Non-invasive ventilation may be considered where appropriate (e.g. BiPAP while asleep).
e) Consider mandatory minute ventilation (MMV) to trend the patient's ability to generate the target volume.

5. Criteria for extubation

a) Optimal conditions: patient completes an extubation readiness trial, tidal volumes > 5 mL/kg, gag and cough are intact.
b) Consider a prolonged extubation readiness trial or trial with minimal ventilator support (PS and PEEP only) to evaluate for fatigability.
c) Patients with poor handling of secretions are at high risk for re-intubation.
d) Consider transitioning to a non-invasive mechanical support after extubation (e.g. BiPAP).

6. Criteria for tracheostomy

a) Prolonged intubation is associated with an increased risk for infection.
b) Patients with extensive bulbar weakness, profound weakness involving the upper extremities and neck and/or diaphragmatic dysfunction may be at increased risk for prolonged respiratory failure and thus benefit from tracheostomy.

II. Bowel and Bladder dysfunction:

Patients with AFM are at increased risk for gut dysmotility, bladder dysfunction/atonia.

1. Patients may benefit from early introduction of a bowel regimen.
2. Bladder distention and prolonged periods between urination may be a sign of a neurogenic bladder. Consider evaluation with a bladder scanner, post void residual and/or scheduled in and out catheterization (preferred over indwelling Foley).

III. Pain:

Patients with AFM are at high risk for pain/allodynia. Pain may be under-recognized. Assess for pain in patients with irritability, refusal to participate in therapy and/or tachycardia.

1. Recognition of and treatment for pain/allodynia may allow for reduced exposure to sedating medications and improved cooperation with therapy/early mobilization. Anecdotally, gabapentin has been effective in reducing pain in AFM patients. Consider starting pain medications early and titrating to effect.
2. Dysautonomia/dysrythmias can occur. Monitoring is recommended.
3. Anxiety may accompany pain and exacerbate the pain symptoms. Low dose benzodiazepines may be a useful adjunct to pain medications in some patients.
4. For patients with incomplete eye closure, order scheduled lacrilube to prevent corneal abrasions. Corneal abrasions are also a source of pain.
5. Early mobilization/therapy may help minimize pain and secondary injuries associated with immobilization and weakness.

IV. Rehabilitation during the intensive care unit stay:

1. Early mobilization may help to promote functional improvement, reduce complications of immobility, and mitigate the effects of muscle disuse. Strengthening programs can often begin in the ICU.
2. Early involvement of PM&R, physical therapy, and occupational therapy is recommended.

B. Supplementary Recommendations for Electromyography and Nerve Conduction Studies in Acute Flaccid Myelitis

Electrophysiology Sub-Group of the Acute Flaccid Myelitis Working Group
Matthew J. Elrick[1], Michele L. Yang[2], Matthew Harmelink[3], Jonathan B. Strober[4], Emmanuelle Tiongson[5], Peggy Lazerow[6], Jiri Vajsar[7], Jay Desai[5], Jessica R. Nance[1], Thomas O. Crawford[1]
[1] Johns Hopkins School of Medicine, Department of Neurology
[2] University of Colorado, Department of Pediatrics, Section of Neurology
[3] Medical College of Wisconsin, Department of Neurology
[4] University of California, San Francisco, Department of Neurology
[5] Children's Hospital Los Angeles, Division of Neurology
[6] Sinai Hospital, Department of Neurology
[7] Hospital for Sick Children, Division of Neurology

Electromyography and Nerve Conduction Studies (EMG/NCS) are valuable tools in the investigation of neuromuscular disorders and have been applied to the diagnosis and management of Acute Flaccid Myelitis (AFM). However, the pathophysiology of AFM is poorly understood, and EMG/NCS findings in AFM are incompletely characterized. These guidelines, therefore, have a dual purpose:
(1) to provide guidance in the electrodiagnostic evaluation of a patient with suspected AFM, and
(2) to standardize the performance of EMG/NCS for the collection of data that will be comparable across institutions and provide clinical data for research purposes.

I. Uses

EMG/NCS has been used for several purposes in AFM. The most common has been diagnostic confirmation. Although EMG/NCS are not required to make a diagnosis of AFM, electrophysiology may be a useful adjunctive test in patients with atypical features and with delayed presentations. Furthermore, EMG/NCS may be useful in the acute setting where the differential diagnosis for an individual patient includes other acute neuromuscular disorders such as Guillain-Barre Syndrome or botulism. All cases reporting EMG/NCS in patients AFM have demonstrated some combination of diminished compound motor action potential (CMAP) amplitudes, fibrillation potentials and positive sharp waves, and reduced voluntary motor unit potential (MUP) recruitment in the absence of sensory nerve conduction abnormalities.[1-7] These findings are consistent with motor neuropathy or neuronopathy. Radiculopathy would also be consistent with the electrophysiology, but is excluded on clinical grounds.

Many centers have used EMG/NCS in pre- and/or post-surgical assessment for nerve transfer procedures. In this setting, EMG/NCS is used to identify the degree of denervation of affected muscles and the relative preservation of innervation by donor nerves. There is additional interest in the use of EMG/NCS for prognostication. One prior study of long-term outcomes suggested EMG/NCS may be a useful predictor.[2] However, questions remain regarding the timing of EMG when used for this purpose, and which measures have the most reliable prognostic value.

II. Questions for investigation

The exact anatomic pattern and extent of EMG abnormalities in AFM remains incompletely characterized. A better understanding of the patterns of motor neuron injury may improve our understanding of viral entry into and spread within the spinal cord. EMG/NCS may help in characterizing the extent of injury. Prior observations in poliomyelitis suggest that poliovirus may have had a stronger propensity to spread within the vertical columns of the anterior horn than spreading laterally within the segment; whether this is true in AFM remains uncertain. Whether motor weakness requires the death of motor neurons or simply disease-induced motor neuron dysfunction is also unknown, but has important implications for treatment and recovery. EMG/NCS early in the disease course may further elucidate the physiology underlying motor deficits. Serial EMG may demonstrate the return of MUPs where there originally were none, suggesting a phase of disease when motor neurons are dysfunctional but not irreversibly injured. Finally, the prognostic value of EMG is suspected, but incompletely investigated. Which EMG/NCS findings correlate best with motor recovery and the optimal timing of such a study has not been demonstrated.

III. Timing of Study

EMG/NCS findings evolve over time, and will therefore yield different information at different timepoints. It should be noted that EMG/NCS may be normal early in the course of the disease. The earliest finding is reduced

recruitment of voluntary motor unit potentials (MUP), which may be found at the time of symptoms onset. Distal CMAP amplitude may decline as early as 5-7 days. Fibrillations and positive sharp waves could take up to three weeks to develop, but have been observed as early as seven days. Chronic changes associated with sprouting and reinnervation, including increased MUP amplitude, duration, and polyphasia, develop next. Improvements in MUP recruitment might occur at this stage as well. We therefore propose that EMG/NCS studies be categorized as follows:

1. Acute: 1-3 weeks following onset of weakness
2. Subacute: 4-8 weeks
3. Chronic: ≥3 months

IV. Selection of nerves and muscles, data to report

EMG studies should be individualized based on patient presentation. The exact selection of nerves and muscles to study should be at the discretion of the electromyographer based upon the patient's pattern of weakness and any specific clinical questions. Where EMG/NCS is performed as part of the diagnostic work-up, we propose a "minimal" study sufficient to support the diagnosis of AFM, and an "ideal" study that should be pursued to optimally characterize the extent and severity of injury. The "ideal" study is also designed to capture data to support the investigation of clinical research questions as discussed above. Data should generally be reported as per custom of the performing laboratory. However, we recommend at least the following standardized features to be included in the report.

1. Minimal study

   Nerve Conduction studies

   a) At least one motor nerve, including proximal and distal stimulation sites. Select a nerve that innervates a weak muscle when able. Report at least the following measures:
      i. CMAP amplitude
      ii. Distal latency
      iii. Conduction velocity
      iv. F wave latency
   b) At least one sensory nerve in an affected limb ideally in the same root distribution of the above motor nerve tested if possible. Report at least the following measures:
      i. SNAP amplitude
      ii. Conduction velocity
      iii. Latency

   Electromyography

   a) For patients with ≥3 limb involvement or hemiplegia:
      i. One distal and one proximal muscle in one affected upper limb and one affected lower limb.
   b) For patients with monoplegia, bilateral upper extremity, or bilateral lower extremity involvement:
      i. one distal and one proximal muscle in each affected limb.
   c) Report at least the following measures.
      i. Fibrillations: graded 0 to 4+
      ii. Positive sharp waves: graded 0 to 4+
      iii. Recruitment pattern: normal, mildly reduced, severely reduced, or no units
      iv. MUP amplitude: graded -4 to +4
      v. MUP duration: graded -4 to +4

2. Ideal study

   Nerve Conduction Studies

   a) At least two motor nerves, including proximal and distal stimulation sites. Select nerves that innervate a weak muscle when able. For research subjects, inclusion of median and ulnar nerves of affected upper extremity limbs and peroneal and tibial nerves of lower extremity limbs is recommended. Report at least the following measures:
      i. CMAP amplitude
      ii. Distal latency
      iii. Conduction velocity

iv. F wave latency

b) At least two sensory nerves in an affected limb ideally in the same nerve and root distribution of the above motor nerves tested, if possible. Report at least the following measures:
   i. SNAP amplitude
   ii. Conduction velocity
   iii. Latency

Electromyography

a) In each affected limb:
   i. At least one affected proximal and one affected distal muscle
   ii. At least one affected flexor and one affected extensor muscle
b) When <4 limbs are involved, also sample at least one clinically unaffected muscle, corresponding to the most severely affected muscle in the opposite limb.
c) Report at least the following measures.
   i. Fibrillations: graded 0 to 4+
   ii. Positive sharp waves: graded 0 to 4+
   iii. Recruitment pattern: normal, mildly reduced, severely reduced, or no units
   iv. MUP amplitude: graded -4 to +4
   v. MUP duration: graded -4 to +4
   vi. Any other spontaneous activity not indicated above

V. Patients being evaluated for nerve transfer surgery

Collaboration between the surgeon and electromyographer in advance of EMG/NCS is highly recommended. Studies should be performed during the chronic phase and after evaluation by the surgeon whenever possible. The selection of muscles to study by EMG will depend on the specific surgical approach(es) being considered. Most commonly, in addition to the guidelines above, the study will include the potential acceptor muscle(s) and at least one muscle innervated by each potential donor nerve.

References

1. Elrick MJ, Gordon-Lipkin E, Crawford TO, et al. Clinical Subpopulations in a Sample of North American Children Diagnosed With Acute Flaccid Myelitis, 2012-2016. *JAMA Pediatr.* 2018.
2. Martin JA, Messacar K, Yang ML, et al. Outcomes of Colorado children with acute flaccid myelitis at 1 year. *Neurology.* 2017;89(2):129-137.
3. Hovden IA, Pfeiffer HC. Electrodiagnostic findings in acute flaccid myelitis related to enterovirus D68. *Muscle Nerve.* 2015;52(5):909-910.
4. Saltzman EB, Rancy SK, Sneag DB, Feinberg Md JH, Lange DJ, Wolfe SW. Nerve Transfers for Enterovirus D68-Associated Acute Flaccid Myelitis: A Case Series. *Pediatr Neurol.* 2018;88:25-30.
5. Knoester M, Helfferich J, Poelman R, et al. Twenty-Nine Cases of Enterovirus-D68 Associated Acute Flaccid Myelitis in Europe 2016; A Case Series and Epidemiologic Overview. *Pediatr Infect Dis J.* 2018.
6. Andersen EW, Kornberg AJ, Freeman JL, Leventer RJ, Ryan MM. Acute flaccid myelitis in childhood: a retrospective cohort study. *Eur J Neurol.* 2017;24(8):1077-1083.
7. Van Haren K, Ayscue P, Waubant E, et al. Acute Flaccid Myelitis of Unknown Etiology in California, 2012-2015. *JAMA.* 2015;314(24):2663-2671.
8. Preston DC, Shapiro BE. Needle electromyography. Fundamentals, normal and abnormal patterns. *Neurol Clin.* 2002;20(2):361-396, vi.

C. Supplementary Recommendations for Rehabilitation in Acute Flaccid Myelitis

Rehabilitation Sub-group of the Acute Flaccid Myelitis Working Group
Janet Dean MS RN CRNP[1], Amy Bayliss MS OTR[2], Megan Blaufuss OTR/L MS CPAM[3], Riley Bove MD, MMSc[4], Glendaliz Bosques MD[5], Kristen Chao MS CCC-SLP CBIS [1], Gabrielle deFiebre MPH,[6] Kaitlin Hagen MOT OTR/L[1], Meghan Moore PT DPT[2], Joyce Oleszek[7], Courtney Porter PT DPT[1], Cristina Sadowsky MD[1,2], Margaret A. Tunney, PsyD[1,8]

1. International Center for Spinal Cord Injury, Kennedy Krieger Institute, Baltimore, Maryland
2. Department of Physical Medicine and Rehabilitation, Johns Hopkins School of Medicine, Baltimore, Maryland
3. Department of Physical and Occupational Therapy, Children's Mercy Hospital, Kansas City, Missouri
4. Department of Neurology, Division of Neuroinflammation and Glial Biology, UCSF MS and Neuroinflammation Center, Weill Institute for Neurosciences, University of California San Francisco, San Francisco, California
5. Department of Physical Medicine and Rehabilitation. McGovern Medical School at UTHealth, Houston, Texas
6. The Siegel Rare Neuroimmune Association, Columbus, Ohio
7. Department of Physical Medicine and Rehabilitation, Children's Hospital Colorado, Aurora, Colorado, USA.
8. Department of Psychiatry and Behavioral Sciences, Johns Hopkins School of Medicine, Baltimore, Maryland.

I. <u>Rehabilitation considerations during the acute illness</u>

1. Rehabilitation Medicine consultation for neurological injury care is recommended. Early initiation of physical, occupational and speech therapy services is essential in the intensive care unit, to address issues related to positioning, progressive and stepwise mobilization, splinting/bracing, communication, and swallowing.[1]
2. Early initiation of electrical stimulation therapy may be helpful to reduce disuse muscular atrophy (although specific studies in AFM are lacking).[2,3,4]
3. Augmentative communication devices and techniques might be needed for relaying pain and discomfort.
4. Children with bulbar involvement or chronic respiratory failure and associated inability to wean from the ventilator will require a tracheostomy and/or a gastrostomy tube and demonstrate stability on a home ventilator for transfer to inpatient rehabilitation.
5. Psychological support should be initiated to assist the child and family through the process of coping and adjustment to the new diagnosis.
6. Medically stable children with moderate to severe residual neurologic deficits should transfer to an inpatient rehabilitation program.[5,6]

II. Early rehabilitation

1. The rehabilitation plan for children with AFM should include short-term goals to facilitate developmentally-appropriate functional independence and the use of compensatory devices, while simultaneously working towards long-term goals for recovery of function and avoidance of musculoskeletal complications including muscle atrophy, bone mass loss, joint contractures, hip and/or shoulder subluxation, limb length inequality and scoliosis.
2. Intensive activity based therapy interventions should be tailored to the individual patient, and may include some of the following: weight loading of upper and lower limbs, locomotor gait training, massed practice with high count repetitions, task specific practice and functional electrical stimulation (FES).[7]
3. Weight loading across a joint with the goal to promote proper joint alignment and muscle co-contraction surrounding the joint[8] can be achieved in the upper limbs via propping on extended arms or forearms while in sitting, standing, prone, side lying, quadruped, or kneeling; lower limbs weight bearing is completed by standing, kneeling, FES cycling, or quadruped positions.
4. Patients who are unable to weight bear on their own can be provided assistance from a therapist, bracing, or other external supports. Supported static and dynamic standers, standers with glider components to allow reciprocal upper and lower extremity movement, and body weight supported standing in harness systems can be utilized where necessary, and depending on the patient's age and abilities.[9]
5. Locomotor gait training (LT) includes interventions aimed at retraining neural patterns to improve walking by providing specific sensory cues.[10] LT focuses on proper gait kinematics, full joint loading, and avoiding compensatory motions or devices.[11] LT is shown to improve trunk strength and neuromuscular capacity in pediatric patients after spinal cord injury (even in non-ambulatory children).[12] However, there is a lack of

evidence regarding the potential benefit or otherwise of LT in patients with AFM - in whom the pathophysiology of neurological injury is quite different. LT sessions can include facilitation over the treadmill, over ground, and carryover activities intended for the patient to practice outside of therapy.

6. Task specific practice - the completion of specific motor tasks to improve motor learning - should be goal directed and be associated with massed practice (high number of repetitions).[13] Children participate in task specific practice activities including activities of daily living (ADL), instrumental activities of daily living (iADL), transfer training, developmental transitions, and mat mobility skills daily in therapy. The tasks should be repeated multiple times a day, over multiple days, to improve strength, range of motion, and increase independence as cortical reorganization responds to non-use as much as it does to use and training.
7. FES can be used in conjunction with the above therapeutic modalities to facilitate muscle contraction in weak or partially denervated muscles. The motor response to electrical stimulation is noted to be decreased in patients with AFM due to lower motor neuron injury. Additionally, most patients with AFM present with intact sensation, which can limit their tolerance to the intensity required to achieve a motor response.
    i. The most successful applications of FES for this kind of injury is the use a low frequency and long pulse width, which allows for time for the slower moving motor units to respond with greater refractory periods.[14]
    ii. Frequency can typically range from 20-40Hz; beginning at a high frequency and decreasing as tolerated by the patient.
    iii. Pulse width can be optimized by motor response, up 3000 microseconds in some software programs; typical home units will have a maximum pulse width of 300-400 microseconds.
8. Activity based therapy principles can also be applied in the aquatic setting and can include developmental play and positioning, standing, kneeling, quadruped and sitting. Aquatic LT is possible with use of an underwater treadmill and/or assistance from a therapist.[15]
9. The plan of care should also include evaluation for orthotic devices, mobility equipment, adaptive equipment, and assistive technology for communication; identification of home care needs, a plan for school and community reentry, psychosocial support, and training for the child and family.[16]
10. Children with poor recovery in an affected muscle group or diaphragm greater than 3 months after onset should be considered for potential nerve transfer surgery by a center experienced in the relevant procedures. The appropriate timing for nerve transfer surgery is uncertain, but a delay in consideration may result in a missed window of opportunity as muscle viability wanes with extended periods of denervation.[17] Tendon transfer surgery - which is not time sensitive - may be considered months or years after initial onset of AFM.[18]

III. Long-Term Management

1. Because AFM predominantly affects young, growing children[16] and improvements over time have been demonstrated,[7,16,19,21,22] continued rehabilitation with periodic bouts of skilled activity based therapy should be provided to aid the acquisition of developmentally appropriate milestones and functional independence.
2. Interdisciplinary reevaluation with review of medical management and rehabilitation goals should occur every 3-4 months during the first year, and every 6-12 months during subsequent years. This includes a review and update of orthotic devices, trials of new equipment for mobility, progressing age appropriate ADLs and communication, and updates to home/community rehabilitation programs.
3. Ongoing specialty care, including neurology, physiatry and orthopedic surgery will be focused on prevention and management of musculoskeletal conditions including muscle atrophy, joint and soft tissue contractures, scoliosis, shoulder and/or hip subluxation,[23] limb length discrepancies, and loss of bone mineral density.[24]
4. The children with significant residual bulbar paralysis and impaired breathing may require pulmonology, otolaryngology and speech language pathology care for prevention and management of complications including respiratory insufficiency, recurrent pneumonia, sleep disordered breathing, ventilator weaning/transition to non-invasive ventilation and speech dysfunction.[25,26]
5. Children with tracheostomy may benefit from trials of a speaking valve (in line with ventilator tubing or capping the tracheostomy) to augment communication.
6. Children with dysarthria might benefit from oromotor, vocal and respiratory strengthening, and education on speech intelligibility strategies.

7. Evaluation and treatment of dysphagia may include diet modifications and implementation of swallowing and behavior strategies. Instrumented assessment of swallowing including modified barium swallow study (MBBS) and/or fiberoptic endoscopic evaluation of swallowing (FEES) may be needed.[27]

References

1. Trovato MK, Bosques G, Grahm RJ, Kramer ME, Pidcock FS, Prestwich, SV, Sadowsky CL. *Rehabilitation*. In Nichols DG, Shaffner DH, eds. Rogers' Textbook of Pediatric Critical Care Medicine. 5th edition. Philadelphia, PA: Wolters Kluwer; 2016:196-207.
2. Needham DM, Truong AD, Fan E. Technology to enhance physical rehabilitation of critically ill patients. Crit Care Med. 2009;37(10 Suppl):S436–S441. i:10.1097/CCM.0b013e3181b6fa29
3. Salmons S, Ashley Z, Sutherland H, Russold MF, Li F, Jarvis JC. Functional electrical stimulation of denervated muscles: basic issues. Artif Organs. 2005;29(3):199–202. doi:10.1111/j.1525-1594.2005.29034.x
4. Mödlin M, Forstner C, Hofer C, et al. Electrical stimulation of denervated muscles: first results of a clinical study. Artif Organs. 2005;29(3):203–206. doi:10.1111/j.1525-1594.2005.29035.x
5. Parent S, Barchi S, LeBreton M, Casha S, Fehlings MG. The impact of specialized centers of care for spinal cord injury on length of stay, complications, and mortality: a systematic review of the literature. J Neurotrauma. 2011;28(8):1363–1370. doi:10.1089/neu.2009.1151
6. Wilson P, Dichiaro, M, Matthews D. Rehabilitation (2014). In Vogel LC, Zebracki K, Betz RR, Mulkahey MJ, eds. Spinal Cord Injury in the Child and Young Adult. London, Mac Keith Press; 2016:297-306. ISBN: 9781909962354
7. Melicosta ME, Dean J, Hagen K, et al. Acute flaccid myelitis: Rehabilitation challenges and outcomes in a pediatric cohort. J Pediatr Rehabil Med. 2019;12(3):245–253. doi:10.3233/PRM-180549
8. Dolbow DR, Gorgey AS, Recio AC, et al. Activity-Based Restorative Therapies after Spinal Cord Injury: Inter-institutional conceptions and perceptions. Aging Dis. 2015;6(4):254–261. Published 2015 Aug 1. doi:10.14336/AD.2014.1105
9. Paleg GS, Smith BA, Glickman LB. Systematic review and evidence-based clinical recommendations for dosing of pediatric supported standing programs. Pediatr Phys Ther. 2013;25(3):232–247. doi:10.1097/PEP.0b013e318299d5e7
10. Harkema SJ, Hillyer J, Schmidt-Read M, Ardolino E, Sisto SA, Behrman AL. Locomotor training: as a treatment of spinal cord injury and in the progression of neurologic rehabilitation. Arch Phys Med Rehabil. 2012;93(9):1588–1597. doi:10.1016/j.apmr.2012.04.032
11. Harkema SJ, Behrman AL, Barbeau H. Locomotor Training: Principles and Practice. Oxford, New York: Oxford University Press; 2011.
12. Behrman AL, Argetsinger LC, Roberts MT, Stout D, Thompson J, Ugiliweneza B, Trimble SA. Activity-Based Therapy Targeting Neuromuscular Capacity After Pediatric-Onset Spinal Cord Injury. Top Spinal Cord Inj Rehabil. 2019. Spring;25(2):132-149. doi: 10.1310/sci2502-132. PubMed PMID: 31068745; PubMed Central PMCID: PMC6496965.
13. Hubbard IJ, Parsons MW, Neilson C, Carey LM. Task-specific training: evidence for and translation to clinical practice. Occup Ther Int. 2009;16(3-4):175–189. doi:10.1002/oti.275
14. Gorgey AS, Black CD, Elder CP, Dudley GA. Effects of electrical stimulation parameters on fatigue in skeletal muscle. J Orthop Sports Phys Ther. 2009;39(9):684–692. doi:10.2519/jospt.2009.3045
15. Li C, Khoo S, Adnan A. Effects of aquatic exercise on physical function and fitness among people with spinal cord injury: A systematic review. Medicine (Baltimore). 2017 Mar;96(11):e6328. doi: 10.1097/MD.0000000000006328.
16. Bove R, Rowles W, Carleton M, Olivera E, Sheehan M, Werdal HP, Scott R, Axton L, Benson L. Unmet Needs in the Evaluation, Treatment, and Recovery for 167 Children Affected by Acute Flaccid Myelitis Reported by Parents Through Social Media. Pediatr Neurol. 2020 Jan;102:20-27. doi:10.1016/j.pediatrneurol.2019.08.009. Epub 2019 Aug 24. PubMed PMID: 31630913.
17. Pino PA, Intravia J, Kozin SH, Zlotolow DA. Early results of nerve transfers for restoring function in severe cases of acute flaccid myelitis. Ann Neurol. 2019;86(4):607–615. doi:10.1002/ana.25558
18. Doi K, Sem SH, Hattori Y, Sakamoto S, Hayashi K, De la Red-Gallego MA. Surgical Reconstruction for Upper-Extremity Paralysis Following Acute Flaccid Myelitis. *JB JS Open Access*. 2019;4(4):e0030. Published 2019 Oct 24. doi:10.2106/JBJS.OA.19.00030
19. Martin JA, Messacar K, Yang ML, et al. Outcomes of Colorado children with acute flaccid myelitis at 1 year. Neurology. 2017;89(2):129–137. doi:10.1212/WNL.0000000000004081

20. Kirolos A, Mark K, Shetty J, Chinchankar N, Mcdougall C, Eunson P, Stevenson J, Templeton K; NHS Lothian EV-D68 Associated AFM Study Group. Outcome of paediatric acute flaccid myelitis associated with enterovirus D68: a case series. Dev Med Child Neurol. 2019 Mar;61(3):376-380. doi: 10.1111/dmcn.14096. Epub 2018 Nov 12. PubMed PMID: 30417347.
21. Yea C, Bitnun A, Robinson J, Mineyko A, Barton M, Mah JK, Vajsar J, Richardson S, Licht C, Brophy J, Crone M, Desai S, Hukin J, Jones K, Muir K, Pernica JM, Pless R, Pohl D, Rafay MF, Selby K, Venkateswaran S, Bernard G, Yeh EA. Longitudinal Outcomes in the 2014 Acute Flaccid Paralysis Cluster in Canada. J Child Neurol. 2017 Mar;32(3):301-307. doi:10.1177/0883073816680770. Epub 2016 Dec 20. PubMed PMID: 28193112.
22. Andersen EW, Kornberg AJ, Freeman JL, Leventer RJ, Ryan MM. Acute flaccid myelitis in childhood: a retrospective cohort study. Eur J Neurol. 2017 Aug;24(8):1077-1083. doi:10.1111/ene.13345. Epub 2017 Jun 22. PubMed PMID:28639345.
23. McCarthy JJ, Chafetz RS, Betz RR, Gaughan J. Incidence and degree of hip subluxation/dislocation in children with spinal cord injury. J Spinal Cord Med.2004;27 Suppl 1:S80-3. PubMed PMID: 15503707.
24. Lauer R, Johnston TE, Smith BT, Mulcahey MJ, Betz RR, Maurer AH. Bone mineral density of the hip and knee in children with spinal cord injury. J Spinal Cord Med. 2007;30 Suppl 1:S10-4. PubMed PMID: 17874680; PubMed Central PMCID: PMC2031968.
25. Alexiou S, Piccione J. Neuromuscular disorders and chronic ventilation. Semin Fetal Neonatal Med. 2017;22(4):256–259. doi:10.1016/j.siny.2017.04.001
26. Arens R, Muzumdar H. Sleep, sleep disordered breathing, and nocturnal hypoventilation in children with neuromuscular diseases. Paediatr Respir Rev. 2010;11(1):24–30. doi:10.1016/j.prrv.2009.10.003
27. Lawlor CM, Choi S. Diagnosis and Management of Pediatric Dysphagia: A Review [published online ahead of print, 2019 Nov 27]. JAMA Otolaryngol Head Neck Surg. 2019;10.1001/jamaoto.2019.3622. doi:10.1001/jamaoto.2019.3622

Supplementary Recommendations for Psychosocial Support for Children and Families

Margaret A. Tunney, PsyD[1,3], Riley Bove, MS, MMSc[2] and the Rehabilitation Subgroup of the Acute Flaccid Myelitis Working Group

1. International Center for Spinal Cord Injury, Kennedy Krieger Institute, Baltimore, Maryland
2. Department of Neurology, Division of Neuroinflammation and Glial Biology, UCSF MS and Neuroinflammation Center, Weill Institute for Neurosciences, University of California San Francisco, San Francisco, California
3. Department of Psychiatry and Behavioral Sciences, Johns Hopkins School of Medicine, Baltimore, Maryland.

Psychosocial support can be critical for the emotional and behavioral well-being of the child, siblings and caregivers.[1,2] Children with AFM most often present with anxiety (e.g. procedural, separation, generalized) and behavioral dysregulation which may lead to variable participation in therapies and cares. Fear, pain, fatigue, diminished functional control, and communication barriers contribute to the manifestation of distress behaviors. Caregivers may experience acute and persistent emotional distress related to their child's sudden loss of function. In addition, they face significant barriers including delays in diagnosis, uncertainty about cause or etiology, lack of qualified resources, lack of insurance coverage, employment impact, and protracted hospitalizations.[16] Healthy siblings can experience uncertainty and sibling relationship may be impacted. As AFM may impact all facets of life with the potential for life long symptoms and impairments, the evaluation of mood and the provision of skills for coping and adjustment are very important not only during the entire hospitalization, but also for the transition to home, school, and the community. Children and caregivers will benefit from ongoing psychosocial support for educational and developmental transitions, mastery of age appropriate self-advocacy skills, increasing independence in self-care, and increasing responsibility for medical management to aid a successful transition to adulthood.

I. Psychosocial Support for Children and Families

1. Incorporate preferred interests and items into therapy sessions and systematically increase task demands.

2. Provide intermittent opportunities for control through choice such as allowing the child to choose the order of therapy activities.
3. Utilize differential attention (i.e. positive praise for adaptive behaviors and planned ignoring of maladaptive behaviors) for behavior management. Targeted reinforcement programs may be considered.
4. Procedural anxiety may occur during various interventions such as tracheostomy changes, ventilator weaning, PMV and capping trials, electrical stimulation, etc. Utilize desensitization to medical and therapy equipment, pre-determined and structured goals, and developmentally appropriate procedural education.
5. Separation anxiety may include crying and frequent requests for the caregiver, repositioning, suctioning, etc. Educate caregivers on intervention including notification of departure and anticipated return, a brief separation process, and return at pre-determined time. Systematically increase frequency and duration of separation over time.
6. Provide relaxation and coping skills training (e.g. diaphragmatic breathing, guided imagery, brave statements) for distress. For younger children, include caregivers so they can assist with prompts and generalization of strategies throughout the day.
7. Provide support for caregiver coping and adjustment as they grieve the sudden and chronic changes in their child's functioning. Specialized education and peer support may also be beneficial for caregiver coping.
8. Teach families how to use modifications to play such as adaptive equipment or hand-over-hand support to engage in games and activities. Teaching healthy siblings new and adapted ways to play with their affected sibling may positively impact sibling relationships.
9. Encourage caregivers to consistently schedule individual time with healthy siblings.
10. Provide brief education regarding AFM to the child and their siblings in developmentally appropriate terminology. In preparation for return to home, school, and community environments, consider developing social scripts for the child to talk about their condition and hospital admission.

References

1. Bove R, Rowles W, Carleton M, Olivera E, Sheehan M, Werdal HP, Scott R, Axton L, Benson L. Unmet Needs in the Evaluation, Treatment, and Recovery for 167 Children Affected by Acute Flaccid Myelitis Reported by Parents Through Social Media. Pediatr Neurol. 2020 Jan;102:20-27. doi:10.1016/j.pediatrneurol.2019.08.009. Epub 2019 Aug 24. PubMed PMID: 31630913.
2. Martin JA, Messacar K, Yang ML, et al. Outcomes of Colorado children with acute flaccid myelitis at 1 year. Neurology. 2017;89(2):129–137. doi:10.1212/WNL.0000000000004081

Supplemental table 1. Summary of data published in large case series relating to proposed diagnostic criteria for acute flaccid myelitis

	California cohort	Canada cohort	CDC cohort 2014	CDC non-peak cohorts 2015 & 2017	Japan cohort	Europe cohort	CDC peak cohorts 2016 & 2018	Total
Authors	Van Haren *et al*	Yea *et al.*	Sejvar *et al*	McLaren et al	Chong *et al*	Knoester *et al*	McLaren *et al*	-
Years of case occurrence	2012-2015	2014	2014	2015 & 2017	2015	2016	2016 & 2018	2012-2018
Region	California, USA	Nationally, Canada	Nationally, USA	Nationally, USA	Nationally, Japan	Multiple European countries	Nationally, USA	-
Case ascertainment	Statewide public health surveillance	Participating centers	National event-based surveillance	National public health surveillance	National event-based surveillance	Collaborating centers	National public health surveillance	-
Age criterion for inclusion	None	<18 years	<22 years	<22 years	None	None	<22 years	-
Number of cases	59	25	120	50	59	29	366	708
Adult cases	9 of 59 (15%)	NA	NA	NA	4 of 59 (7%)	3 of 29 (10%)	NA	16 of 147 (11%)
Median age, years (range)	9 (0.5-73)	7.8 (0.8-15.0)	7.1 (0.4-20.8)	8.3 (0.3-20.2)	4.4 (0-80)	4 (1.6-55)	5.2 (0.4-21.9)	-
Males/Females	33/26	16/9	71/49	32/18	35/24	15/14	217/149	419/289
Factors suggestive of AFM								
H1: Acute onset of limb weakness	59 of 59 (100%)[a]	25 of 25 (100%)[a]	120 of 120 (100%)[a]	50 of 50 (100%)[a]	59 of 59 (100%)[a]	29 of 29 (100%)[a]	366 of 366 (100%)[a]	708 of 708 (100%)[a]
H2: Prodromal fever or viral illness	54 of 59 (92%)	22 of 25 (88%)	105 of 117 (90%)	31 of 50 (62%)	57 of 59 (97%)	26 of 29 (90%)	328 of 366 (90%)	621 of 702 (88%)
E1: Weakness involving one or more limbs	59 of 59 (100%)[a]	25 of 25 (100%)[a]	120 of 120 (100%)[a]	50 of 50 (100%)[a]	59 of 59 (100%)[a]	29 of 29 (100%)[a]	366 of 366 (100%)[a]	708 of 708 (100%)[a]
E1: Weakness involving neck, face and/or bulbar muscles	16 of 59 (27%)	7 of 25 (28%)	34 of 120 (28%)	10 of 50 (20%)	10 of 59 (17%)	17 of 28 (60%)	96 of 366 (26%)	190 of 707 (27%)
E2: Decreased muscle tone in affected limbs	59 of 59 (100%)[a]	25 of 25 (100%)[a]	NR	50 of 50 (100%)[a]	59 of 59 (100%)[a]	NR	366 of 366 (100%)[a]	534 of 534 (100%)[a]
E3: Decreased or absent tendon reflexes in weak limb(s)	59 of 59 (100%)[a]	22 of 25 (88%)	97 of 120 (81%)	NR	53 of 59 (90%)	20 of 22 (87%)	NR	95 of 106 (90%)
MRI: Spinal cord lesion with predominant gray matter involvement with or without root enhancement	56 of 59 (95%)	25 of 25 (100%)[a]	120 of 120 (100%)[a]	50 of 50 (100%)[a]	58 of 59 (98%)	23 of 25 (92%)	366 of 366 (100%)[a]	698 of 704 (99%)
CSF: Pleocytosis (white cell count >5 cell/uL)	43 of 58 (74%)	18 of 25 (72%)	91 of 112 (81%)	28 of 47 (60%)	40 of 42 (95%)[b]	20 of 22 (91%)	283 of 328 (86%)	523 of 634 (82%)
Factors suggestive of an alternative diagnosis								
Encephalopathy/altered mental status (unspecified etiology)	13 of 59 (22%)	1 of 25 (4%)	12 of 109 (11%)	NR	7 of 59 (12%)	NR	NR	33 of 252 (13%)
Presence of unspecified sensory abnormalities	26 of 59 (44%)	3 of 25 (12%)	NR	NR	NR	NR	NR	27 of 84 (32%)

Supratentorial white matter or cortical lesions	7 of 48 (15%)[c]	2 of 25 (8%)	11 of 104 (11%)	NR	1 of 56 (2%)	0 of 25 (0%)	NR	30 of 261 (12%)
AQP4-IgG positive	NR	NR	NR	NR	0 of 27 (0%)	NR	NR	0 of 27 (0%)
MOG-IgG positive	NR	NR	NR	NR	0 of 8 (0%)	NR	NR	0 of 8 (0%)

H=history, E=examination, NR=not reported, NA=not applicable, AQP4=aquaporin-4, MOG=myelin oligodendrocyte glycoprotein.
[a]Used as a criterion to define cases in these studies. [b]CSF study was completed within 5 days of neurological symptom onset in these patients. [c]5 patients had T2-hyperintense lesion(s) in the white matter, and 2 patients had DWI abnormalities in the splenium of the corpus callosum. Denominators are provided for each variable, to account for data that was missing or not tested.
Studies reporting ≥25 cases of AFM are included in this table.[1, 5, 6, 12, 34, 69] Of note, data from the US is based on reports from the Centers for Disease Control and Prevention (CDC) which has been tracking confirmed cases since 2014. The largest series of US cases captured prior to CDC surveillance is also included here,[1] but notably 24 of the 59 cases reported in that study did overlap with CDC reports and therefore there is some duplication of data between the California cohort and CDC cohort.[1, 69] Other publications of case series based on US populations since 2014 have not been included here, as it is likely that most of these cases have been captured by CDC reports covering the same periods. Methodology for the definition and validation of cases differed across these studies. All included studies required the acute onset of focal limb weakness for case inclusion. The presence of a spinal cord gray matter lesion was an inclusion criterion for all the CDC cohorts and the Canada cohort; whereas the Japan cohort and Europe cohort included patients without an MRI lesion where there was CSF pleocytosis; and the California cohort included patients without an MRI lesion where there was electromyogram evidence of anterior horn cell damage. Additionally, detection of enterovirus-D68 in a respiratory, fecal, blood or CSF specimen using validated PCR was an inclusion criterion for the Europe cohort, but not in the other cohorts.

Supplemental table 2. Paraclinical investigations during the recovery phase of AFM

Electromyography (EMG)/Nerve conduction studies (NCS)
• EMG/NCS can be considered on an individualized basis and may have utility in supporting a diagnosis, defining the extent of injury or planning therapy. The timing and anatomical distribution of studies should be adjusted for the patient's weakness pattern and the purpose of the study. • Characteristic findings on EMG/NCS may emerge as early as one week after onset of weakness. • The use of EMG/NCS for defining areas of injury, prognosis and supporting the development of a long-term rehabilitation plan is likely most reliable at least 3 weeks after onset of weakness. • Children (and families) vary in their ability to tolerate extensive EMG/NCS studies. Sedation, anxiolysis, or analgesia may be appropriate, though sedation may undermine assessment of voluntary motor unit recruitment. • We propose an **early** minimal study sufficient to demonstrate motor neuropathy/neuronopathy consistent with a diagnosis of AFM, and a **later** ideal study to best delineate the pattern and extent of neurologic injury (Supplemental Table 2).
MRI
• Follow-up MRI in the recovery phase can be considered on an individualized basis and may have utility in demonstrating areas of residual injury and establishing a new imaging baseline. • In the weeks after onset of AFM, spinal cord edema improves and T2 signal in some (or all) regions of the gray matter will return to normal, while in some regions the anterior horns on one or both sides of the spinal cord may demonstrate residual well-defined areas of T2 hyperintensity. White matter abnormalities resolve. Spinal nerve root enhancement may persist for weeks to months. • Areas of residual anterior gray matter T2 hyperintensity may correlate with persistent weakness of muscles innervated by those anterior horn cells.

Supplemental table 3. Recommendations regarding evaluation of AFM with electromyography/nerve conduction studies

	Minimal study	Ideal study	Measures to include/report	Characteristic findings
NCS	• At least 1 motor nerve (proximal and distal stimulation), ideally innervating a weak muscle • At least 1 sensory nerve in an affected limb, ideally in the same root distribution as the tested motor nerve • Where nerve transfer surgery is being considered, potential donor nerve(s) should be tested	• At least 2 motor nerves (proximal and distal stimulation), ideally innervating weak muscles • At least 2 sensory nerves in an affected limb, ideally in the same root distribution as the tested motor nerves • Where nerve transfer surgery is being considered, potential donor nerve(s) should be tested	• Motor: CMAP amplitude, distal latency, conduction velocity, F wave latency • Sensory: SNAP amplitude, conduction velocity, latency	• Diminished or absent CMAPs • Normal sensory NCS
EMG	• If ≥3 affected limbs or hemiplegia: test 1 distal and 1 proximal muscle in 1 affected upper limb and 1 affected lower limb • If monoplegia, bilateral upper extremity, or bilateral lower extremity involvement: test 1 distal and 1 proximal muscle in each affected limb • Where nerve transfer surgery is being considered, potential acceptor muscle(s) should be tested	• In each affected limb: test at least 1 distal and 1 proximal muscle, at least 1 flexor and 1 extensor muscle • If ≤3 limbs are involved, also sample at least one clinically unaffected limb (using a muscle corresponding to the most severely affected muscle in the opposite limb) • Where nerve transfer surgery is being considered, potential acceptor muscle(s) should be tested	• Fibrillations: graded 0 to 4+ • Positive sharp waves: graded 0 to 4+ • Recruitment pattern: normal; mildly reduced; severely reduced; no units • MUP amplitude: graded -4 to 4+ • MUP duration: graded -4 to 4+	• Early: reduced or absent recruitment of MUPs • Subacute (1-3 weeks): fibrillations and positive sharp waves • Chronic (weeks to months): progressively increasing MUP amplitude and duration consistent with denervation/reinnervation, fibrillations and positive sharp waves gradually diminish but may persist for months to years

NCS=nerve conduction studies, EMG=electromyography, CMAP=compound motor action potentials, SNAP=sensory nerve action potentials, MUP=voluntary motor unit potential

Acute Flaccid Myelitis Working Group members and institutions

Ann & Robert H. Lurie Children's Hospital of Chicago, Northwestern University Feinberg School of Medicine, Chicago, IL, USA,
Sue Hong, MD., Division of Pediatric Critical Care,
Divakar S Mithal, MD., Division of Neurology.

Boston Children's Hospital, Harvard Medical School, Boston, MA, USA,
Leslie Benson, MD., and **Molly Wilson-Murphy, MD.,** Department of Neurology,
Andrea Bauer, MD., and **Colyn Watkins, MD.,** Department of Orthopaedic Surgery.

Children's Healthcare of Atlanta, Emory University School of Medicine, Atlanta, GA, USA,
Grace Y. Gombolay, MD., Department of Neurology.

Children's Hospital Colorado, University of Colorado School of Medicine, Aurora, CO, USA, **Mark J. Abzug, MD., Samuel R. Dominguez, MD.,** and **Kevin Messacar, MD.,** Section of Pediatric Infectious Diseases,
Joyce Oleszek, MD., Department of Physical Medicine and Rehabilitation,
Craig Press, MD PhD., Section of Child Neurology,
Teri L. Schreiner, MD., and **Michele Yang, MD.,** Department of Neurology.

Children's Hospital Los Angeles, Los Angeles, CA, USA,
Nusrat Ahsan MD., **Jay Desai, MD**., **Leigh Ramos-Platt, MD.,** and **Emmanuelle Tiongson, MD.,** Division of Neurology,
Mitchel Seruya, MD., Division of Plastic and Maxillofacial Surgery.

Children's Hospital New Orleans, Louisiana State University, New Orleans, LA, USA,
Ann Tilton, MD., Departments of Neurology and Pediatrics.

Children's Hospital of Philadelphia, Department of Pediatrics, Philadelphia, PA, USA,
Sarah E. Hopkins, MD., Division of Neurology,
Elana Katz, MD., Division of Rehabilitation Medicine,
Matthew Kirschen, MD., Department of Anesthesiology and Critical Care Medicine,
Apurva S. Shah, MD., Division of Orthopaedics,
Erlinda R. Ulloa, MD., Division of Infectious Disease,
Sabrina W. Yum, MD., Department of Neurology.

Children's Hospital of Wisconsin, Milwaukee, WI, USA,
Raquel Farias-Moeller, MD., **Matthew Harmelink, MD**., and **Lileth J. Mondok, MD.,** Department of Neurology.

Children's Mercy Hospital, Kansas City, MO, USA,
Megan Blaufuss OTR/L MS CPAM. Department of Physical and Occupational Therapy.

Children's National Health System, Washington, DC, USA,
Jessica L. Carpenter, MD., and **Elizabeth M. Wells, MD.,** Department of Neurology,
Roberta DeBiasi, MD., Division of Pediatric Infectious Diseases.

Columbia University Vagelos College of Physicians and Surgeons, New York, NY, USA,
Amy B. Rosenfeld, PhD., , Department of Microbiology and Immunology.

Columbia Irving University Medical Center, New York, NY, USA,
Kiran T. Thakur, MD., and **Wendy Vargas., MD.,** Department of Neurology,
Jason Zucker, MD., Departments of Internal Medicine and Pediatrics.

Icahn School of Medicine at Mount Sinai, New York, NY, USA.

Anusha K. Yeshokumar, MD., and **Allison P. Navis, MD.,** Department of Neurology.

International Center for Spinal Cord Injury, Kennedy Krieger Institute, Baltimore, MD, USA, **Kristen Chao MS CCC-SLP CBIS, Janet Dean, MS RN CRNP, Kaitlin Hagen MOT OTR/L, Michelle Melicosta, MD., Courtney Porter PT DPT, Cristina L. Sadowsky, MD**., and **Margaret A. Tunney, PsyD.**

J. Craig Venter Institute, La Jolla, CA, USA,
Richard H. Scheuermann, PhD.

Johns Hopkins Bloomberg School of Public Health, Baltimore, MD, USA,
Priya Duggal, PhD., Department of Epidemiology,
Andrew Pekosz, PhD., Department of Molecular Microbiology and Immunology.

Johns Hopkins University School of Medicine, Baltimore, MD, USA,
Amy Bayliss MS OTR, and **Meghan Moore PT DPT.**, Department of Physical Medicine and Rehabilitation,
Allan Belzberg, MD., ., Department of Neurosurgery,
Melania M. Bembea, MD PhD., Caitlin O'Brien, MD., and **Rebecca Riggs, MD**., Department of Anesthesiology and Critical Care Medicine,
Thomas O. Crawford, MD., Matthew J. Elrick, MD PhD., and **Jessica R. Nance, MD** Department of Neurology and Pediatrics, Division of Neurology,
Aaron M. Milstone, MD MHS, Department of Pediatrics, Division of Infectious Diseases
Jessica L. Rice, DO., Department of Pediatrics, Division of Pulmonology,
Olwen C. Murphy, MBBCh, MRCPI, Maria A. Garcia, MD, Carlos A. Pardo, MD., and **Andrea Salazar-Camelo, MD.,** Department of Neurology, Division of Neuroimmunology and Neurological Infections.

Mayo Clinic College of Medicine, Rochester, MN, USA,
Eoin P. Flanagan, MBBCh., and **Jan-Mendelt Tillema, MD.,** Department of Neurology.

McGovern Medical School at UTHealth, Houston, Texas, USA,
Glendaliz Bosques, MD., Department of Physical Medicine and Rehabilitation.

Medical University of South Carolina, Charleston, SC, USA,
Sonal Bhatia, MD., Department of Neurology.

National Human Genome Research Institute, Metabolism, Infection and Immunity Section, National Institutes of Health, Bethesda, MD, USA,
Eliza Gordon-Lipkin, MD.

Seattle Children's Hospital, Seattle, WA, USA,
Catherine Otten, MD. , Department of Pediatric Neurology.

Shirley Ryan Ability Lab, Chicago, IL, USA,
Dawn Deike, MD., and **Gadi Revivo, DO.,** Pediatric Physical Medicine and Rehabilitation.

Shriners Hospital for Children Philadelphia, Philadelphia, PA, USA,
Dan A. Zlotolow, MD., Department of Orthopaedic Surgery.

Siegel Rare Neuroimmune Association, Columbus, Ohio,
Gabrielle deFiebre MPH.

Sinai Hospital of Baltimore, Baltimore, MD, USA,
Peggy Lazerow, MD., Division of Pediatric Neurology.

Stanford University School of Medicine, Palo Alto, CA, USA,
Keith van Haren, MD., Department of Neurology and Neurological Sciences.

Texas Children's Hospital, Houston, TX, USA,
Timothy E. Lotze, MD., Department of Neurology.

The Hospital for Sick Children, Department of Pediatrics, University of Toronto, Ontario, Canada, **Ari Bitnun, MD.,** Division of Infectious Diseases,
Kristen M. Davidge, MD., Division of Plastic and Reconstructive Surgery,
Jiri Vajsar, MD, and **E. Ann Yeh, MD MA.,** Division of Neurology, Department of Pediatrics.

The Ohio State University, Nationwide Children's Hospital, Columbus, OH, USA,
Amy Moore, MD., Department of Plastic and Reconstructive Surgery.

University of California, San Diego, San Diego, CA, USA,
Chamindra Konersman, MD., Department of Neurosciences.

University of California, San Francisco, San Francisco, CA, USA,
Riley Bove, MD., **Kendall Nash, MD** and **Jonathan B. Strober, MD.,** Department of Neurology,
Nalin Gupta, MD., Department of Neurological Surgery,
Charles Chiu, MD PhD., Department of Medicine, Division of Infectious Diseases.

University of Louisville and Norton Children's Hospital, Louisville, KY, USA,
Michael L. Sweeney, MD., Department of Neurology.

University of Maryland School of Medicine, Baltimore, MD, USA,
William T. Jackson, PhD., Department of Microbiology and Immunology.

University of Pittsburgh Medical Center Children's Hospital of Pittsburgh, Pittsburgh, PA, USA, **Dennis W. Simon, MD. ,** Departments of Critical Care Medicine and Pediatrics,
Kavita Thakkar, MD., Department of Pediatrics, Division of Child Neurology.

University of Texas Southwestern Medical Center, Dallas, TX, USA,
Jonathan Cheng, MD., Department of Plastic Surgery,
Benjamin Greenberg, MD., Department of Neurology.

Valley Children's Hospital, Madera, CA, USA,
John Luce, DO., Department of Pediatric Physical Medicine and Rehabilitation.

Vanderbilt University Medical Center, Nashville, TN, USA,
Suman R. Das, PhD., Division of Infectious Diseases, Department of Medicine,
Matthew R. Vogt, MD PhD., Division of Infectious Diseases, Department of Pediatrics,
NgocHanh Vu, MD., Department of Neurology.

Weill Cornell Medical College, New York, NY, USA,
Jacqueline S. Gofshteyn, MD., Department of Neurology.

Yale University School of Medicine, New Haven, CT, USA,
Naila Makhani, MD., and **Payal Patel, MD.**, Department of Neurology.

International Collaborative Group for AFM Research
Argentina
Hospital de Niños "Ricardo Gutiérrez," Buenos Aires, Argentina,
Carolina M. Carballo, MD., and **Eduardo L. Lopez, MD**., Department of Infectious Diseases.

India
Indira Gandhi Institute of Child Health, Bangalore, Karnataka, India,
Vykuntaraju K. Gowda, DM., Division of Pediatric Neurology.

Japan
Fukuoka Children's Hospital, Fukuoka, Japan,
Pin Fee Chong, MD., and **Ryutaro Kira, MD PhD.,** Department of Pediatric Neurology.

Netherlands
University Medical Center Groningen, University of Groningen, Groningen, The Netherlands,
Jelte Helfferich, MD., Department of Neurology.

United Kingdom
Evelina London Children's Hospital, Guy's and St Thomas' NHS Trust, London, U.K,
Ming Lim, MD PhD., Children's Neuroscience Center.

Senegal
Institut Pasteur de Dakar, Dakar, Senegal,
Amary Fall, PhD., Département de Virologie.