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MEDICINE

Acute Flaccid Myelitis: Respiratory considerations in the PICU

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Disclosure

I unfortunately have nothing to disclose

Objectives

1. Supportive Measures to Prevent Intubation
2. Identifying Respiratory Failure
3. Suggested Criteria for Intubation and Extubation
4. Suggested Criteria for Tracheostomy
5. Procedural sedation vs. Prolonged Sedation to support Intubation
6. Acute Pain Management of patients with AFM

Most are Acutely at Risk for Developing Respiratory Failure!

- Phrenic and cardiac innervation at C3-C5
  - Respiratory failure; autonomic instability!
- EV-D68 infection has been associated with poorer outcomes with AFM.
  - Greater risk of permanent neurological injury and prolonged respiratory failure requiring tracheostomy.
- Severe weakness at the peak of illness appears to predict poor prognosis for full recovery.

TABLE 1.
Patient Characteristics — Acute Impatient — 21 Total

Characteristics	No. (%)
Age at onset (median, range)	5 years (6.8 months, 15 years)
Illness course and symptoms	
Sensory deficit*	1 (5)
Pain	12 (57)
Cranial nerve palsies	7 (33)
Change in mental status on exam	5 (24)
Respiratory failure	7 (33)

33%

TABLE 1.
Demographic Characteristics of the Acute Inpatient Phase — Acute Inpatient — 167 Total

Variables	Survey 1	Survey 2	Surveys Combined	CDC 120[15,32]
Demographics				
Age, median (S.D.) [age at survey]	7 (6.14)	7 (5.78)	7 (5.91)	7.1 (0.4-20.8)
Gender		N = 104		N = 120
Male		63 (60.6%)		71 (59.2%)
Female		41 (39.4%)		49 (40.8%)
Sitting up	37 (63.8%)	77 (76.2%)	114 (71.7%)	NR
Walking	44 (75.9%)	78 (77.2%)	122 (76.7%)	NR
Respiratory difficulties	31 (53.5%)	53 (52.5%)	84 (52.8%)	95/118 (80.5%)

80%

TABLE 4.
Persistent Deficits in Children Affected by AFM at a Mean Duration of 2.4 Years Since AFM Onset. Current Deficits at the Time of the Survey (Surveys 1 and 2)

Symptoms	Survey 1 (N = 46)	Survey 2 (N = 83)	Total (N = 129)
Vision — 2.4 Years Later	4 (8.7%)	10 (12.0%)	14 (10.9%)
Face	6 (13.0%)	10 (12.0%)	16 (12.4%)
Swallowing	5 (10.9%)	15 (18.1%)	20 (15.5%)
Neck	11 (23.9%)	27 (32.5%)	38 (29.5%)
Walking	32 (50.0%)	43 (51.8%)	**75 (58.1%)**
Pain (in location of onset, e.g., neck or hips; and back of the knees)	21 (45.7%)	30 (36.1%)	51 (39.5%)
Respiratory difficulties	7 (15.2%)	21 (25.3%)	28 (21.7%)

22%

Millichap JG. Acute flaccid myelitis outbreak. Pediatr Neurol Briefs. 2015;29:96.

Chong P, Kira R, Mori H, et al. Clinical features of acute flaccid myelitis temporally associated with an enterovirus D68 outbreak: results of a nationwide survey of acute flaccid paralysis in Japan, August-December 2015. Clin Infect Dis. 2018;66:653e664.

Downey R, McElvain D, Murphey DK, Bailey A, Patel B, Fernandez M, Loftis L, Carreno CG, Eger L, Aguilera EA, Wootton S, Castagnini LA, Hauger SB.Downey R, et al. Acute Flaccid Myelitis Among Hospitalized Children in Texas, 2016. *Pediatr Neurol.* 2020 May;106:50-55. 2020.

> Pediatr Neurol. 2020 Jan;102:20-27. doi: 10.1016/j.pediatrneurol.2019.08.009. Epub 2019 Aug 24.

Unmet Needs in the Evaluation, Treatment, and Recovery for 167 Children Affected by Acute Flaccid Myelitis Reported by Parents Through Social Media

Riley Bove [1], William Rowles [2], Mia Carleton [2], Erin Olivera [3], Mikell Sheehan [4], Heather P Werdal [5], Rachel Scott [6], LaMay Axton [7], Leslie Benson [8]

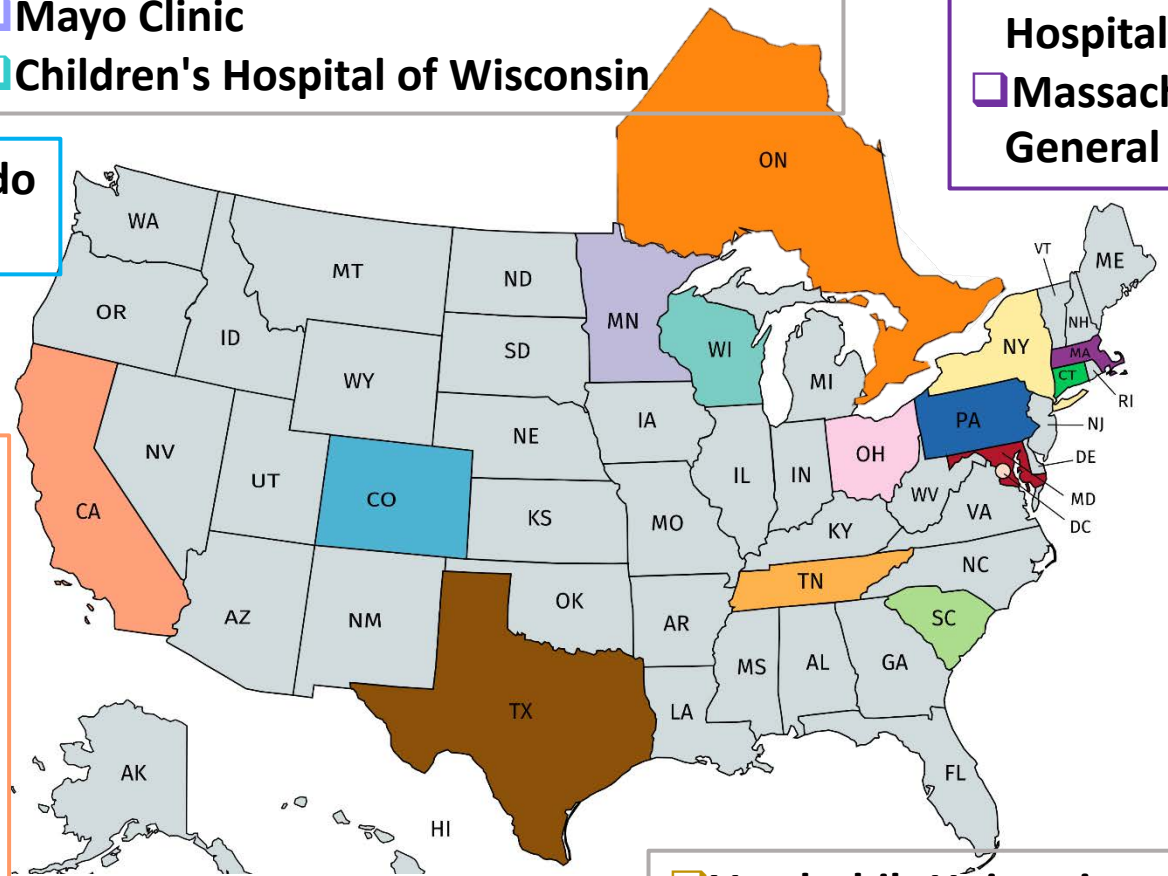
- Closed media Facebook group with 167 Affected Children:
  - Average initial hospitalization was 49 days (SD 74)
  - Initial inpatient rehabilitation was 42 days (SD 68)
  - Acutely 80% suffered respiratory difficulties
    - Chronically only 22% suffered respiratory difficulties
  - Almost 25% of children required tracheostomy
    - Average duration of tracheostomy was 15.3 months
  - Many children were able to wean off the ventilator after about 6 months
    - Of the 36 children who were ventilator dependent in 2014 only 3 remained dependent in 2018.

More Questions than Answers with AFM

- Most of our knowledge of AFM is based on anecdotal experience, and small to medium-sized case series.
- AFM remains poorly understood in terms of its etiology, pathophysiology, clinical course, biomarkers, treatment and outcomes.
- The ambiguity of whether we are dealing with an active infectious process or a post infectious inflammatory process, gives rise to controversy in the use of immunomodulatory and/or antiviral therapies.
- Coordinated research efforts to collate data from a large number of cases across multiple institutions are essential to close these knowledge gaps and provide evidence-based care to these young patients.

AFM Working group Network

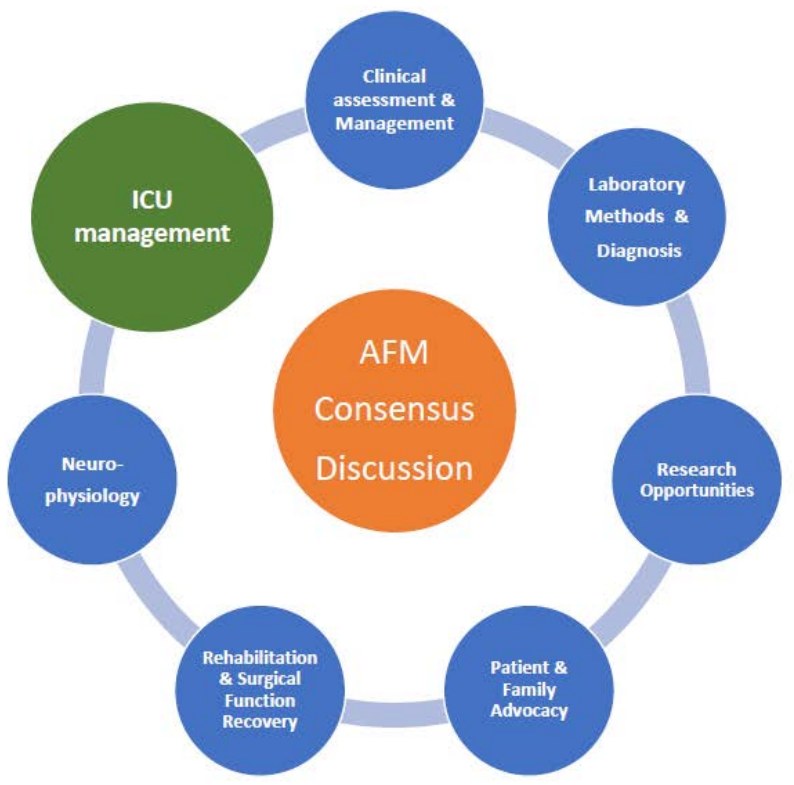
- Transverse Myelitis Association
- The Hospital for Sick Children, University of Toronto
- Mayo Clinic
- Children's Hospital of Wisconsin
- Columbia University
- Weill Cornell School of Medicine
- Mt. Sinai Hospital
- Boston Children's Hospital
- Massachusetts General Hospital
- Children's Hospital Colorado
- University of Colorado
- Yale School of Medicine
- Children's Hospital of Philadelphia
- University of Pennsylvania



- UCSF Benioff Children Hospital
- Kaiser Permanente San Francisco Medical Center
- Stanford University
- Children's Hospital Los Angeles
- J. Craig Venter Institute
- Children's National Medical Center (DC)
- Johns Hopkins University School of Medicine
- Johns Hopkins Bloomberg School of Public Health
- Kennedy-Krieger Institute
- Sinai Hospital
- National Institutes of Health
- UT Southwestern: Neurology; Neurotherapeutics; Pediatrics
- Vanderbilt University Medical Center
- Medical University of South Carolina

Empiric Recommendations for PICU Management of AFM

- Development of a PICU sub-committee as a part of the larger AFM workgroup
- Weekly international phone calls from October 2018 to January 2019
- Monthly international phone calls ongoing
- Multi-disciplinary contributions from 15 institutions
  - Pediatric Intensivists
  - Pediatric Neuro-Intensivists
  - Pediatric Neurology
  - Pediatric Physical Medicine and Rehabilitation



Respiratory Failure

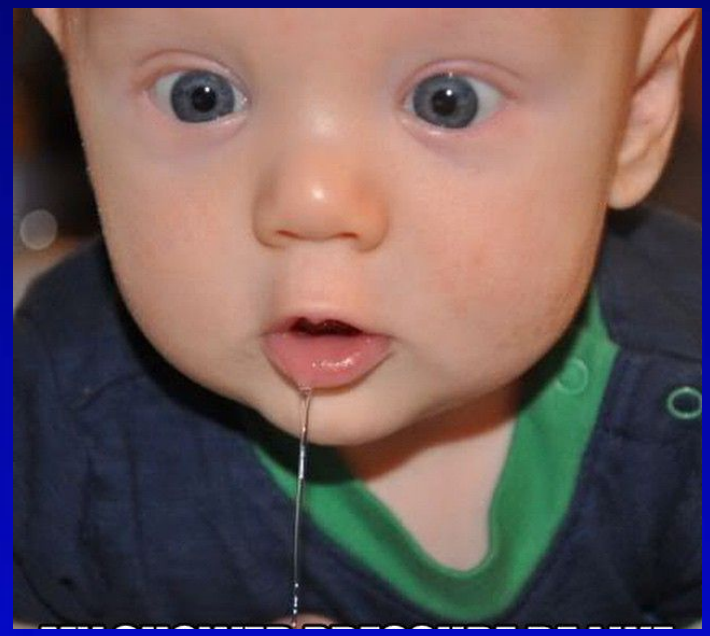
Respiratory failure is most often from hypoventilation secondary to weakness or bulbar weakness impeding airway protection.

- When AFM is suspected, the first and most important step is to be sure that the patient's airway is protected!
- Pediatric Intensive Care Unit admission should be considered for close neurologic monitoring, particularly for patients with cervical lesions (C3-5) given the possibility of respiratory deterioration and the risk of autonomic instability!
- Close monitoring for respiratory suppression is essential during the diagnostic work-up.
- Supportive care remains the mainstay of acute treatment for AFM.

Respiratory Failure

Respiratory failure is most often from hypoventilation secondary to weakness or bulbar weakness impeding airway protection.

- Identify High Risk Patients:
  - Poor head control
  - Drooling
  - Loss of vocalization
  - Inability to raise arms above head
- Monitoring:
  - End Tidal CO2 side stream; pulse ox
  - > 6 years old
    - Q 4 hr Negative Inspiratory Force (NIFs) and Forced Vital Capacity (VFC)
  - < 6 years old
    - Sing a song, hum, count, on a single breath q 4 hours



Respiratory Failure

Supportive Measures to Minimize the Risk of Respiratory Failure:

- Early mobilization (PT/OT and PM&R)
- Aggressive Pulmonary Toilet:
  - Frequent suctioning
  - Chest PT, Cough Assist
  - Inhaled Nebs and mucolytics as indicated
- Aggressive screening for and treatment of co-infections
- Minimize: Sedatives, sleep aides
- Avoid: Magnesium, Paralytics, Steroids, Opioids
- Formal swallowing evaluation prior to initiation of oral diet
- Aggressive support with non-invasive ventilation (BiPAP while asleep)

Respiratory Failure

Suggested thresholds for intubation:

- Intubation thresholds similar for all Neuromuscular weakness (Guillain Barre, Botulism, SMA, Transverse Myelitis, Myasthenia)
  - Vital capacity ≤20 mL/kg
  - NIF less than -30 cmH_2O
  - $paCO_2$ to ≥50 mmHg
  - Desaturation and/or O2 requirement
  - Sweating of the head/neck, wide pulse pressure, tachypnea, tachycardia (↑CO_2)
- Inability to swallow or manage secretions
- Highly consider nasal intubation for younger patients (less sedation).
- Consider mandatory minute ventilation (MMV) to trend the patient's ability to generate target volumes.

Respiratory Failure

Criteria for Extubation:

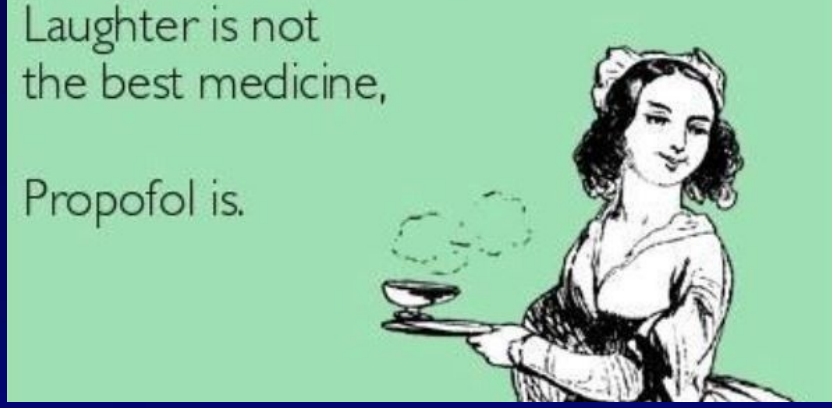
- Patient completes an Extubation Readiness Trial (PS/PEEP only)
  - Intact cough and gag
  - TV > 5 mL/kg, SpO_2 >95%, Ø tachypnea, Ø tachycardia
- Consider a prolonged ERT to evaluate for fatigability
  - (24-48 hours).
- Patients with poor handling of secretions are high risk for re-intubation
- Extubate to aggressive non-invasive mechanical support (BiPAP).

Respiratory Failure

Considerations for early Tracheostomy:

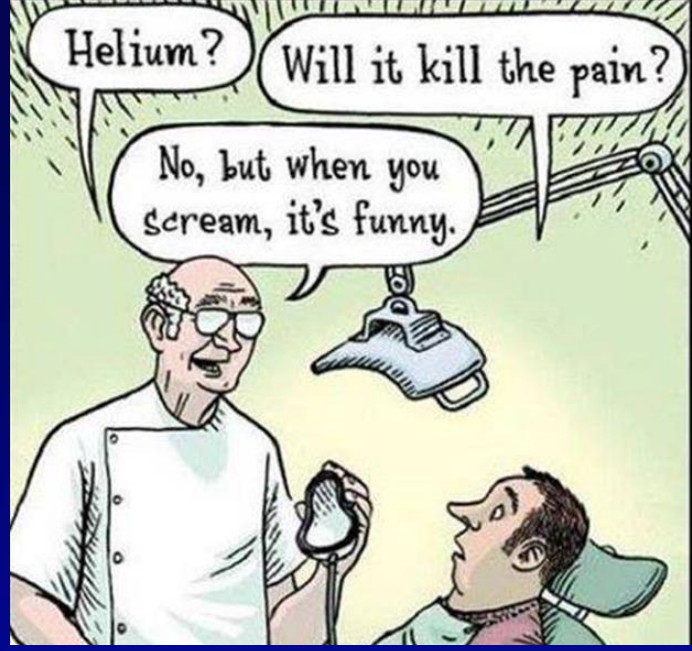
- Failed extubation without new infection x 2
- Early tracheostomy to facilitate early inpatient rehabilitation
- Prolonged intubation has an increased risk for VAPs
- Consider early diaphragmatic pacing as a tracheostomy sparing technique
- Patients with extensive bulbar weakness, profound weakness of the upper extremities, neck and/or diaphragm benefit from early tracheostomy.

Procedural Sedation



- Institutional sedation protocols should be reviewed for potential to increase the risk for respiratory failure.
- Sedated procedures:
  - Provide medications with low risk for respiratory suppression.
    - –Dexmedetomidine, Ketamine, Propofol
  - Use shorter acting agents when opioids and benzodiazepines must be provided.
    - –Fentanyl > Hydromorphone & Midazolam > Diazepam
  - Shorten procedures if possible to minimize sedation
    - –Decrease time in MRI scanner with high yield sequences obtained first
  - Environmental modifications should be optimized to reduce the need for sedation
    - –Child Life, Allowing parents to be present

Intubation Sedation



- Long term sedation requirements are minimal
  - Many do not require continuous infusions
- Medications without respiratory depression are preferred
  - Dexmedetomidine (Autonomic instability)
- Avoid opioids given that pain needs are neuromuscular in nature
  - Constipation; Respiratory depression
- Alternative medications to lessen narcotics and benzodiazepines
  - Clonidine, Gabapentin

Treating AFM Pain

- Pain is often under recognized.
- AFM patients are at high risk for pain/allodynia.
  - Day 1-14 of paralysis: Muscle spasm- Valium
  - Paralysis > 14 days: Nerve pain- Gabapentin
- Assess for pain with tachycardia, irritability, refusal to participate in therapy.
- Recognition of and appropriate treatment of pain/allodynia minimizes exposure to sedating agents and facilitates early mobilization. (Gabapentin)
- Incomplete eye closure, schedule lacrilube to prevent corneal abrasions.

Conclusions

Respiratory failure is most often from hypoventilation secondary to weakness or bulbar weakness impeding airway protection.

- When AFM is suspected, the first and most important step is to be sure that the patient's airway is protected!
- Low threshold to admit to the Pediatric Intensive Care Unit- especially if cervical spinal lesions C3-5.
- When in doubt over-support with non-Invasive BIPAP/CPAP/HFNC especially overnight when sleeping.
- Minimize sedatives and avoid elective intubation for procedures or MRI.
- Prioritize rapid transition to inpatient rehabilitation if available.

References

- Downey R, McElvain D, Murphey DK, Bailey A, Patel B, Fernandez M, Loftis L, Carreno CG, Eger L, Aguilera EA, Wootton S, Castagnini LA, Hauger SB.Downey R, et al. Acute Flaccid Myelitis Among Hospitalized Children in Texas, 2016. *Pediatr Neurol.* 2020 May;106:50-55. 2020. PMID: 32192819
- Bove R, Rowles W, Carleton M, Olivera E, Sheehan M, Werdal HP, Scott R, Axton L, Benson L.Bove R, et al. 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. PMID: 31630913
- Hopkins, Sarah. Acute Flaccid Myelitis: Etiologic Challenges, Diagnositc and Management Considerations. *Curr Treat Options Neurol.*2017 Nov 28;19(12):48.
- Millichap JG. Acute flaccid myelitis outbreak. Pediatr Neurol Briefs. 2015;29:96.
- Chong P, Kira R, Mori H, et al. Clinical features of acute flaccid myelitis temporally associated with an enterovirus D68 outbreak: results of a nationwide survey of acute flaccid paralysis in Japan, August-December 2015. Clin Infect Dis. 2018;66:653e664.
- Downey R, McElvain D, Murphey DK, Bailey A, Patel B, Fernandez M, Loftis L, Carreno CG, Eger L, Aguilera EA, Wootton S, Castagnini LA, Hauger SB.Downey R, et al. Acute Flaccid Myelitis Among Hospitalized Children in Texas, 2016. *Pediatr Neurol.* 2020 May;106:50-55. 2020.

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What we know about treatment in AFM

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