Neuromuscular Disease and Liberation from Mechanical Ventilation
Edward M Manno M.D FNCS, FCCM, FAAN, FANA, FAAN.
Professor of Medicine Cleveland Clinic Lerner College of Medicine Case Western University.

Disclosures
• Financial none
• President of the NeuroCritical Care Society

Neuromuscular disease
• Metamorphosis in this course over last 5-10 years
• Approach these processes from the Neuro intensivists perspective
  – Will not spend a lot of time on the diagnosis
  – Will spend on time on what to do in specific clinical situations.
Neurogenic Respiratory Failure

• Definition
  – Respiratory failure due to difficulties with
    • Motor neurons (Cell bodies)
    • Axons
    • Neuromuscular junction
      – Pre synaptic
      – Post synaptic
    • Muscle
  – Not due to primary pulmonary problems

Neurogenic Respiratory Failure: Overview

• Clinical Presentation
  – Patterns of Weakness
    • Respiratory
    • Bulbar
    • Appendicular
  – Pulmonary function tests
  – Blood gases
  – Timing of intubation

Neurogenic Respiratory Failure: Specific diseases and treatments

• Amyotrophic lateral sclerosis
• Myasthenia Gravis
  – Lambert- Eaton Syndrome
• Guillain-Barre Syndrome
• Critical Illness Neuropathy
• Critical Illness Myopathy
• Other
  – Isolated phrenic neuropathies, plexopathies
  – Rhabdomyolysis, acute myopathies
  – Botulism, tick paralysis
Clinical Presentation

- Generalized fatigue, vague paraesethias, ascending paralysis (GBS)
  - May have been preceded by viral illness or vaccination
- Diplopia, dysphagia, vary degrees of appendicular weakness (MG)
- Progressive dyspnea
- Dysautonomia
  - Fluctuating blood pressure
  - Cardiac arrhythmias

Respiratory weakness

- Neuromuscular weakness
  - Decreased vital capacity compensated by increases respiratory rate
  - Progressive atelectasis
    - Cough weakens
    - Expiratory flow rates decrease
    - Intrinsic sigh is lost
  - Increased work of breathing
    - Exacerbates weakness in MG
    - Cannot be compensated in GBS

Respiratory weakness

- Hypercapnia
  - Late sign
  - Hypoventilation sign of impending Respiratory collapse
Respiratory weakness

- Normal – 65-70 cc/kg Tidal volumes
- Weak cough – 30cc/kg
- Atelectasis – 20-25 cc/kg
- Sigh lost, atelectasis and shunting 15 cc/kg
- Hypoventilation – 10 cc/kg
- Hypercapnia – 5-10 cc/kg

Respiratory weakness

- Arterial blood gases
  - Initial changes
    - Subtle drop in oxygen levels with the development of atelectasis
  - Later changes
    - Mild hypercapnia with normal pH
    - Rapid deterioration with apnea
### Laboratory Values in Monitoring Acute Neuromuscular Failure

<table>
<thead>
<tr>
<th>Measurement</th>
<th>Procedure</th>
<th>Normal value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vital capacity</td>
<td>Max exhalation</td>
<td>40-70 mL/kg</td>
</tr>
<tr>
<td>Maximal inspiratory pressure</td>
<td>Max sucking in</td>
<td>M &gt;-100 cm H₂O</td>
</tr>
<tr>
<td></td>
<td></td>
<td>P &gt;-70 cm H₂O</td>
</tr>
<tr>
<td>Maximal expiratory pressure</td>
<td>Max blowing out</td>
<td>M &gt;200 cm H₂O</td>
</tr>
<tr>
<td></td>
<td></td>
<td>P &gt;140 cm H₂O</td>
</tr>
</tbody>
</table>

### Respiratory weakness

**Respiratory parameters**
- Forced vital capacity
  - Generally intubate if <10cc/kg
  - May be underestimated by respiratory tech
  - Similar flow volume loops as COPD
    - Prolonged tail due to extended exhalation time
  - Count to 30 on one breath
    - Cheap but effective way to estimate VC
    - Approximately 2 Liters
- Neck flexors and proximal muscle strength correlate best with respiratory strength

**Negative Inspiratory Force**
- Better predictor < 20
  - Muscle strength
  - Need for intubation
- Can be underestimated
  - Weak seal around device
  - Facial weakness
    - MG
    - Miller fisher variant of GBS
Respiratory weakness

• Clinical findings (Not all patients will have)
  – Dyspnea
    • VC is half of predicted
  – Brow sweating
  – Accessory muscle use

• INTUBATION SHOULD BE BASED UPON THE CLINICAL PRESENTATION, RATE OF RESPIRATORY DECLINE, AND PULMONARY FUNCTION TESTS
NEUROINTENSIVIST WORRIES

- Respiratory failure (both mechanical and pulmonary)
- Dysautonomia
- Procedure complications (PLEX)

Guillain-Barre Disease (Acute Inflammatory demyelinating polyneuropathy)

- Autoimmune process
  - Effects myelin sheath of peripheral nerves
  - Humoral attack may be induced by viruses, vaccinations
  - Demyelination slows conduction along nerves
    - Leads to progressive weakness
    - Axonal variant

MGH Series

Retrospective Series n=169

- Diarrhea 6%
- Malaise 8%
- Pneumonia 3%
- Surgery 1%
- No prior illness 39%
- Upper respiratory tract infection 8%

Prospective Series n=120

- Diarrhea 10%
- Upper respiratory tract infection 49%
- Pregnancy 1%
- Surgery 8%
- No prior illness 30%
- Upper respiratory tract infection 5%
- CMV 3%
- Pneumonia 2%
- Hodgkin's disease 5%
- SLE vaccination 9%

Ropper, Wijdicks, Truax, 1991
Diagnostic Criteria for GBS

- **Strongly supportive features**
  - Progression of symptoms over 4 weeks
  - Symmetric legs greater than arms weakness
  - Mild sensory symptoms
  - Cranial nerve involvement especially bilateral facial weakness
  - High protein content in the CSF with < 10 cells
  - EMG/NCV: Conduction block, increased F waves and distal latencies

Treatment for GBS

- **Supportive**
  - Respiratory
  - Treat dysautonomia
    - Deafferentate cardiac and baroreceptors
    - Pseudoobstruction
    - DVT prophylaxis
- **Plasma Exchange** *No role for BiPAP in GBS*
- **IVIG**
- **Steroids not helpful**
  - Evaluate for CIDP
Plasma Exchange Trials in GBS

<table>
<thead>
<tr>
<th></th>
<th>North American study</th>
<th>Conventional study</th>
</tr>
</thead>
<tbody>
<tr>
<td>Days to reach grade 2</td>
<td>53</td>
<td>85</td>
</tr>
<tr>
<td>Patient improved at least 1 grade at 6 mo (%)</td>
<td>97</td>
<td>87</td>
</tr>
<tr>
<td>Patients walking independently at 6 mo (%)</td>
<td>82</td>
<td>71</td>
</tr>
</tbody>
</table>

French study

<table>
<thead>
<tr>
<th></th>
<th>n=111</th>
<th>n=109</th>
</tr>
</thead>
<tbody>
<tr>
<td>Days to onset motor recovery (median)</td>
<td>6</td>
<td>13</td>
</tr>
<tr>
<td>Days weaning (median)</td>
<td>18</td>
<td>31</td>
</tr>
<tr>
<td>Days to recover walking without assistance (median)</td>
<td>70</td>
<td>111</td>
</tr>
</tbody>
</table>

Corticosteroid Studies Disability Grade Change After 4 Weeks

<table>
<thead>
<tr>
<th>Study</th>
<th>Control No.</th>
<th>WMD (95% CI fixed)</th>
<th>Weight (%)</th>
<th>WMD</th>
</tr>
</thead>
<tbody>
<tr>
<td>GBS Steroid, 1993</td>
<td>124</td>
<td>87.7</td>
<td>0.070</td>
<td></td>
</tr>
<tr>
<td>Hughes, 1978</td>
<td>21</td>
<td>9.4</td>
<td>-0.500</td>
<td></td>
</tr>
<tr>
<td>Shukla, 1988</td>
<td>6</td>
<td>3.0</td>
<td>-0.210</td>
<td></td>
</tr>
<tr>
<td></td>
<td>151</td>
<td>100.0</td>
<td>0.008</td>
<td></td>
</tr>
</tbody>
</table>

Chi-square 1.44 (df=2) Z=0.06

Hughes. The Cochrane Library (2), 1999

Duration of Ventilation in Recent Large Series

<table>
<thead>
<tr>
<th>Descriptive studies</th>
<th>Ventilated No.</th>
<th>Median duration of ventilation (days)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mayo Clinic 1974-79</td>
<td>79</td>
<td>37</td>
</tr>
<tr>
<td>MGH Prospective 1981-88</td>
<td>85</td>
<td>49</td>
</tr>
<tr>
<td>Queen Square ICU 1985-92</td>
<td>79</td>
<td>21</td>
</tr>
<tr>
<td>Southeast England 1993-94</td>
<td>79</td>
<td>19</td>
</tr>
</tbody>
</table>
**Pulmonary Function Ratio**

\[ PF = \frac{\text{at day 12}}{\text{at intubation}} \geq 1 \]

**Pulmonary Function Score**

\[ \text{VC} + \text{PI max} + \text{PE max} \]

\[ (\text{mL/kg}) \quad (\text{cm H}_2\text{O}) \quad (\text{cm H}_2\text{O}) \]

**Prognosis GBS**

- Depends upon degree and extent of Axonal damage
  - Demyelination alone will recover within days to weeks
  - Axonal damage with intact myelin sheaths will recover within months
  - Most patients will make a complete recovery
    - Psychological support
    - GBS Support groups
Myasthenia Gravis

- Unknown Autoimmune disease forming antibodies to the acetylcholine receptor
- Young women and older men
- 10% thymoma
- Genetic disposition HLA A1, DRW3, B12
- Ocular and appendicular forms

Classification/Diagnosis

- MG Foundation I-V
  - I Ocular, V – Intubated
- Diagnosis
  - >85% ACh antibodies, muscle specific tyrosine kinase antibodies
  - Progressive weakness
  - Decremental EMG pattern, Single fiber jitter
  - Thymoma
  - Edrophonium or neostigmine test
  - Bulbar dysfunction admit to ICU

Causes of Myasthenic Crisis (n=63)

<table>
<thead>
<tr>
<th>Cause</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Myasthenic weakness alone</td>
<td>32</td>
</tr>
<tr>
<td>Respiratory infection</td>
<td>27</td>
</tr>
<tr>
<td>Post thymectomy</td>
<td>17</td>
</tr>
<tr>
<td>No specific therapy</td>
<td>12</td>
</tr>
<tr>
<td>Start of prednisolone therapy</td>
<td>5</td>
</tr>
<tr>
<td>Overdose of cholinergic drugs</td>
<td>3</td>
</tr>
<tr>
<td>Under dose of cholinergic drugs</td>
<td>2</td>
</tr>
<tr>
<td>Emotional stress</td>
<td>2</td>
</tr>
</tbody>
</table>
Pharmaceutical Agents with the Potential to Aggravate Myasthenia Gravis

- **Antibiotics**
  - Clindamycin
  - Colistin
  - Kanamycin
  - Neomycin
  - Streptomycin
  - Tobramycin
  - Tetracycline's
  - Gentamicin
  - Polymyxin B
  - Bacitracin
  - Trimethoprim-sulfamethoxazole

- **Hormones**
  - ACTH
  - Corticosteroids
  - Thyroid hormone
  - Oral contraceptives

- **CV agents**
  - Quinidine
  - Propranolol
  - Procainamide
  - Pranidol
  - Lidocaine
  - Verapamil
  - Nitroglycerin
  - Diltaizem

- **Psychotropic agents**
  - Chlorpromazine
  - Promazine
  - Phenazine
  - Lithium
  - Diazepam

- **Miscellaneous**
  - Penicillamine
  - Chlorpromazine
  - Succinylcholine chloride
  - Catecholamines
  - Benzodiazepines
  - Phentoin
  - Trimethadione
  - Carbamazepine
Initial Management in Patients with Myasthenic Crisis

- Specific treatment
  - Stop pyridostigmine during mechanical ventilation
  - 5 plasma exchanges (2 consecutive days followed by exchanges on alternate days)
  - 5 days of IVIG, 0.4 g/kg
  - Corticosteroids (60 mg/day) if no improvement after 5 days of plasma exchange
  - In refractory cases, cyclosporine (5 mg/kg/day in 2 divided doses) or mycophenolate mofetil (2 g in 2 divided doses)

OUTCOME

- Median ICU stay 11-14 days
- Complications respiratory infections
- Mortality less than 5%
- Cardiac arrhythmias common
- Pulmonary emboli common
- May be able to use BiPAP in some situations

Conclusions

- Healthy ‘RESPECT’ for NM disease
- Intubate early based on PFT’s
- Differentiation is important for longer term care
  - EMG, NCS limits, rep stimulation and single fiber evaluations are useful