



## Pulmonary Function Testing in Neuromuscular Disorders

Terrence Shenfield MS, RRT-  
ACCS, RPFT, NPS, AE-C



# Objectives

- Describe neuromuscular disorders that impact breathing
- Describe different pulmonary function test that can be used in the management of neuromuscular breathing disorders
- Describe test commonly used at the bedside that can determine severity of impairment
- Describe studies on this topic



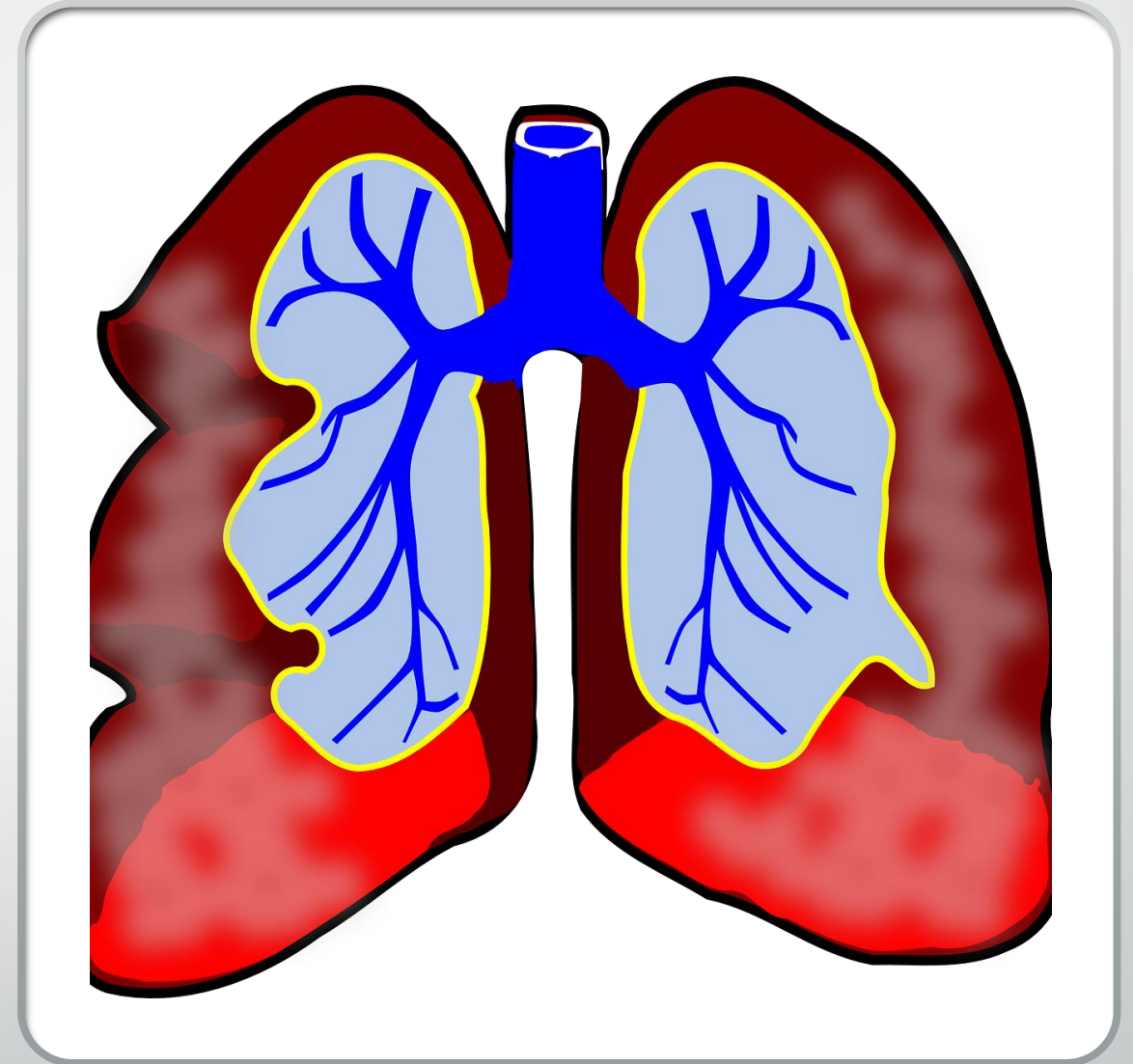
What are  
common  
neuromuscular  
disorders that  
impact  
breathing?

- Amyotrophic lateral sclerosis (ALS)
- Multiple sclerosis
- Muscular dystrophy
- Myasthenia gravis
- Guillain-Barré
- Spinal muscular atrophy
- Chronic inflammatory demyelinating polyneuropathy (CIDP)



# Effects of NMD on the respiratory system

- Respiratory muscle strength
- Cough function
- Sleep abnormalities
- Reduction in respiratory system compliance

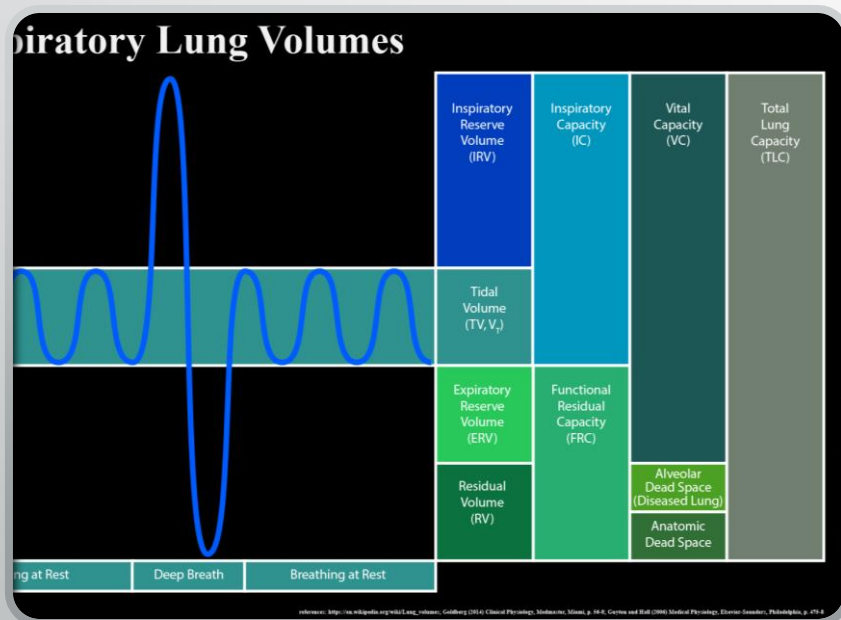


What kind of pulmonary function test are offered for this population?

- Lung Volumes
- Peak Cough Flow
- Spirometry
- Peak flow rate
- Forced vital capacity
- MIP
- MEP
- MIC



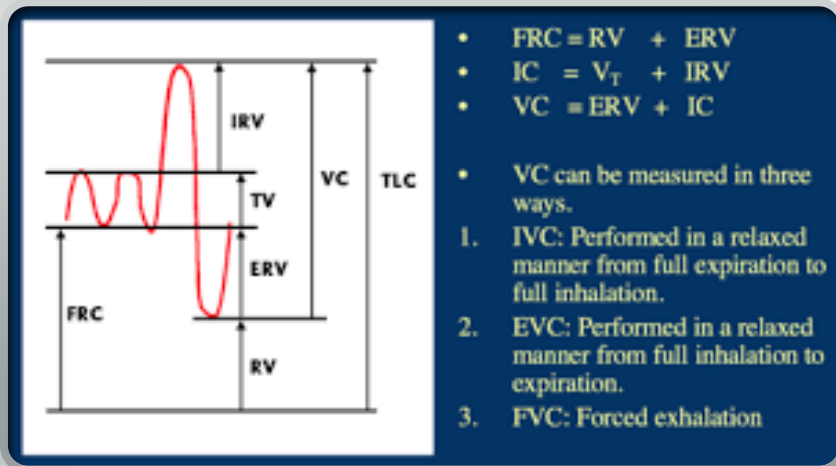
# Lung Volumes- Total Lung Capacity



- Depends on the mechanics of the lungs and chest wall
- TLC is set by the lung's inward recoil and the strength of contraction of the chest muscles.
- Low TLC is the hallmark of a restrictive ventilatory defect
  - Increased lung recoil (interstitial fibrosis)
  - Chest wall abnormality (kyphoscoliosis)
  - Neuromuscular weakness (Duchenne muscular dystrophy, spinal muscular dystrophy)



# Lung Volumes- FRC and RV



- The increased lung recoil is associated with low values for FRC and RV.
- RV is determined by the ability of expiratory muscles to compress the chest wall inward.
- Muscle weakness caused by involvement of expiratory muscles results in elevated values of RV and may be one of the earliest and only findings.
- In neuromuscular weakness, the TLC is low, FRC is normal, and RV is high.
- The FRC and RV may be normal or low in chest wall deformities.



# Peak Flow Rate



- Muscle weakness caused by neuromuscular disorders results in reduced values for peak flow.
- PFR is effort dependent.
- The use of CPF can minimize effort-related variation.
- Patients with neuromuscular weakness, CPF measured by peak flow meter is a better and more reliable measurement of expiratory muscle strength.
  - Inexpensive used to monitor muscle strength at home.
- Assisted CPF measurements, the patient air-stacks as deeply as and can possible and abdominal thrust is applied.
- The difference between assisted and unassisted CPF can be used to measure glottic integrity





# Peak Cough Flow

- **The Peak Cough Flow (PCF) is the maximum air flow generated during a cough.**
- **It is used to assess cough in patients with respiratory muscle weakness, mainly in patients with neuromuscular pathology.**
- **This is done using a flowmeter graduated in Liters/minute.**

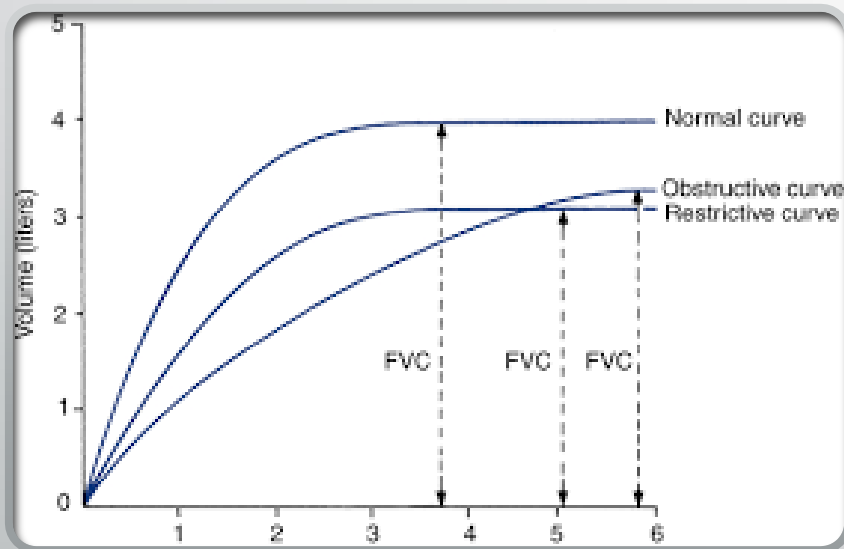


# Peak cough flow (PCF)

- Peak cough flow values lower than  $160 \text{ L}\cdot\text{min}^{-1}$  have been shown to be a good predictor of an ineffective cough and indicate those at risk of developing acute respiratory complications with NMD.



# Forced Vital Capacity



- Neuromuscular disorders (NMD) typically present with mild to severe muscle weakness
- Advancing respiratory muscle weakness leads to progressive pulmonary impairment and reductions in total lung capacity
- Peak cough flow (PCF) and other pulmonary function tests are commonly measured in clinical practice globally, to assess cough effectiveness and document progression of pulmonary impairment in adults and children with NMD



# Maximal inspiratory/expiratory pressure (MIP & MEP)

- Respiratory Muscle Strength MIP and MEP are measured while a patient inhales or exhales maximally against a closed shutter. They are the most sensitive indicators of decreased respiratory muscle strength.
- MIP and MEP are noninvasive, straightforward tests in which individuals are asked to perform a forceful inspiration after an expiration to residual volume level (in the case of MIP) or expiration after a full inspiration to total lung capacity (TLC; in the case of MEP) with an open glottis against an occluded mouthpiece
- MIP may even predict diaphragm weakness before a significant change in spirometry endpoints (eg, forced vital capacity [FVC])



# Maximum Inspiratory Pressure as a clinically meaningful trial endpoint for neuromuscular diseases

- Respiratory muscle strength is a proven predictor of long-term outcome of neuromuscular disease (NMD).
- Maximal inspiratory pressure (MIP) and maximal expiratory pressure (MEP) are direct measures of respiratory muscle strength and may be more sensitive in detecting early respiratory muscle dysfunction compared with spirometry
- MIP and MEP are not usually performed on all patients referred for PFTs
- MIP and MEP are noninvasive, straightforward tests in which individuals are asked to perform a forceful inspiration after an expiration to residual volume level (in the case of MIP) or expiration after a full inspiration to total lung capacity (TLC; in the case of MEP) with an open glottis against an occluded mouthpiece



# Relationship between MIP and survival in patients with NMD

- Respiratory failure is a common cause of premature death in patients with NMD
- Patients with progressive disease require frequent monitoring of their pulmonary function
- Studies have investigated the correlation between MIP and survival in various conditions



# Studies of predicted survival rate using MIP and MEP as predictors

- A cohort study in 95 patients with ALS found a significant association between MIP and 1-year survival ( $P < 0.05$ ). The study found that, whereas a normal ( $>80\%$  predicted) supine FVC predicted a  $> 80\%$  chance of 1-year tracheostomy-free survival, a normal MIP or MEP predicted a  $> 90\%$  chance of survival.
- In a second ALS study, reduced MIP predicted poor 2-years survival.
- In a third study of ALS patients ( $N = 21$ ), MIP ( $-60$  cm H<sub>2</sub>O or less) was 100% sensitive as a “threshold” for predicting 18-months survival, whereas FVC ( $<80\%$  of predicted) was not as sensitive for predicting survival ( $<80\%$  sensitive).
- In a fourth study of 53 patients with ALS, comparison of baseline data in patients who were dead or alive at 18 months showed that survivors had a higher mean MIP ( $38 \pm 24\%$  predicted) than nonsurvivors ( $20 \pm 18\%$  predicted;  $P < 0.01$ ). The absence of cough spikes (defined as peak flow rate transients during voluntary cough) had no significant influence on survival.
- Finally, clinical results from a 5-years prospective, comparative trial of patients with ALS using noninvasive ventilation found that determinants of respiratory function (including MIP [ $P = 0.0001$ ]) were an independent predictor of 5-years survival, emphasizing the potential utility of MIP as a prognostic indicator in patients with ALS.



# Lung insufflation procedures in neuromuscular disease

- Air stacking (Lung inflation capacity)
  - Technique in which a person is encouraged to breathe in slowly at intervals, stacking one breath on top of the other. This technique allows the lungs take in more oxygen than normal inspiration by encouraging the patient to breathe in slowly breathing and stacking one breath on top of other as tolerance allows, followed by a short hold before slow expiration
- Maximum insufflation capacity (MIC)
  - Air stacking was achieved by the patient taking a deep breath, holding it, and then air stacking consecutively delivered volumes of air from a manual resuscitator through the oronasal mask to the maximum volume that could be held with a closed





**Lung  
insufflation  
capacity in  
neuromuscular  
disease  
MIC**

# Lung insufflation capacity in neuromuscular disease study

- To compare maximal passive lung insufflation capacity (LIC) with lung inflation by air stacking (to maximum insufflation capacity [MIC])
- To explore relationships between these variables that correlate with glottic function and cough peak flows (CPF)
- To demonstrate the effect of routine inflation therapy on LIC and MIC; and to determine the relative importance of lung inflation therapy as a function of disease severity.
- Passive lung insufflation can distend the lungs of patients with NMD significantly greater than air stacking, particularly when glottic and bulbar-innervated muscle dysfunction is severe.
- LIC, MIC, and VC measurements permit quantifiable assessment of glottic integrity and, therefore, bulbar-innervated muscle function for patients with NMD.
- The patients who benefit the most from insufflation therapy are those who have the lowest VC.

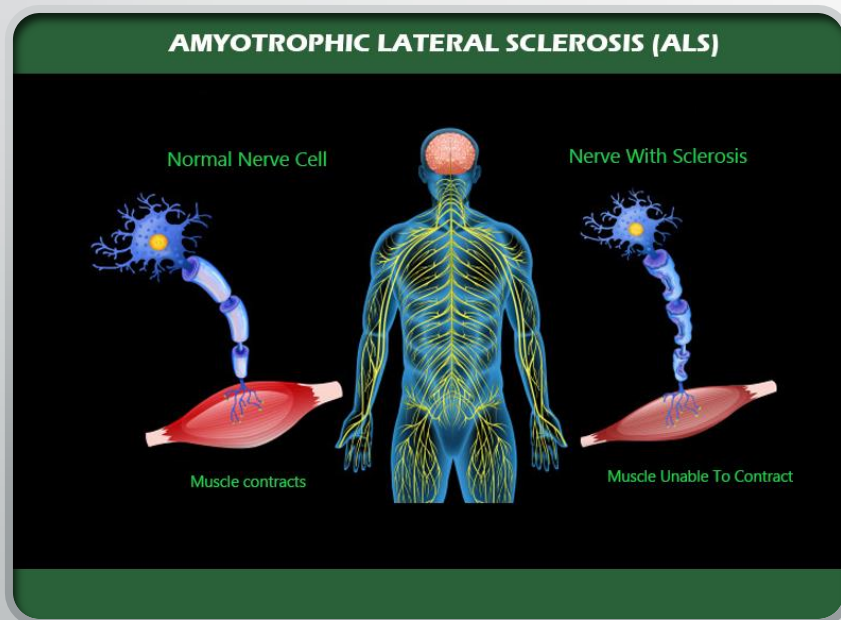


# Let's talk about neuromuscular diseases

- Amyotrophic lateral sclerosis (ALS)
- Multiple sclerosis
- Muscular dystrophy
- Myasthenia gravis
- Guillain-Barré
- Spinal muscular atrophy
- Chronic inflammatory demyelinating polyneuropathy (CIDP)



# Amyotrophic lateral sclerosis (ALS)



- ALS is a disease of the parts of the nervous system that control voluntary muscle movement.
- In ALS, motor neurons are gradually lost. As these motor neurons are lost, the muscles they control become weak and then nonfunctional, thus leading to muscle weakness, disability, and eventually death. ALS is the most common form of motor neuron disease.
- ALS usually strikes in late middle age (the late 50s is average) or later, although it can occur in young adults as well as in very elderly people.
- Some forms of ALS have their onset in youth. Men prior to the age of 65 or 70 are slightly more likely to develop ALS than are women
- The causes of most ALS cases are still unknown. Investigators theorize that some individuals may be genetically predisposed to developing the disease but do so only after encountering an environmental trigger.
- The interaction of genetics and environment may hold clues as to why some individuals develop ALS.



# Multiple sclerosis

- Multiple sclerosis (MS) is an autoimmune disease. With these conditions, your immune system mistakenly attacks healthy cells.
- In people with MS, the immune system attacks cells in the myelin, the protective sheath that surrounds nerves in the brain and spinal cord.
- Damage to the myelin sheath interrupts nerve signals from your brain to other parts of your body.
- The damage can lead to symptoms affecting your brain, spinal cord and eyes.
- Nearly 1 million adults in the U.S. are living with multiple sclerosis.
- MS commonly affects more women than men.
- Most people with MS receive a diagnosis between the ages of 20 and 40.

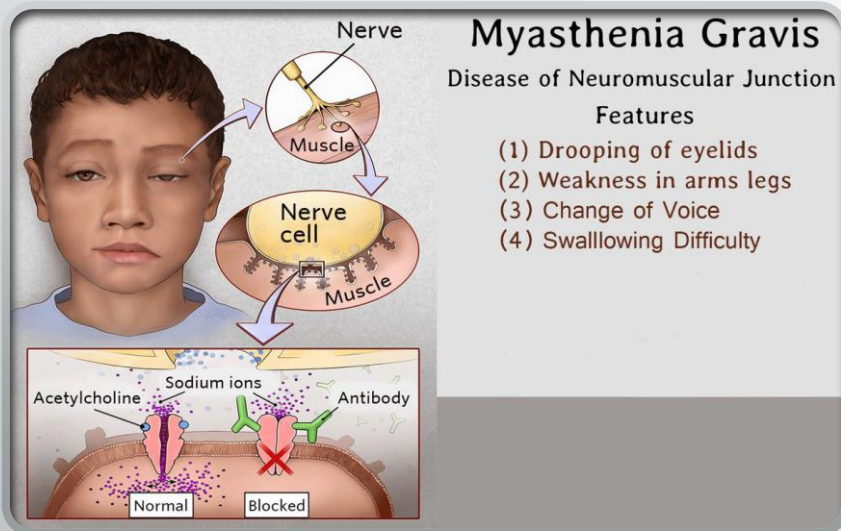


# Muscular dystrophy

- Progressive weakness and degeneration of skeletal muscles caused by genetic alterations fall into the category of muscular dystrophy.
- Muscular dystrophy occurs worldwide and affects all races.
- The overall incidence of muscular dystrophy varies among forms, as some forms are more common than others.
- Muscle loss and weakness are not necessarily caused by genetic alteration.
- Skeletal muscle inactivity, denervation, cancer-associated cachexia, and physiological responses to fasting or malnutrition cause skeletal muscle mass loss through imbalance in synthesis and breakdown of proteins.
- Several genes have been identified that are directly or indirectly involved in various muscle wasting.



# Myasthenia gravis

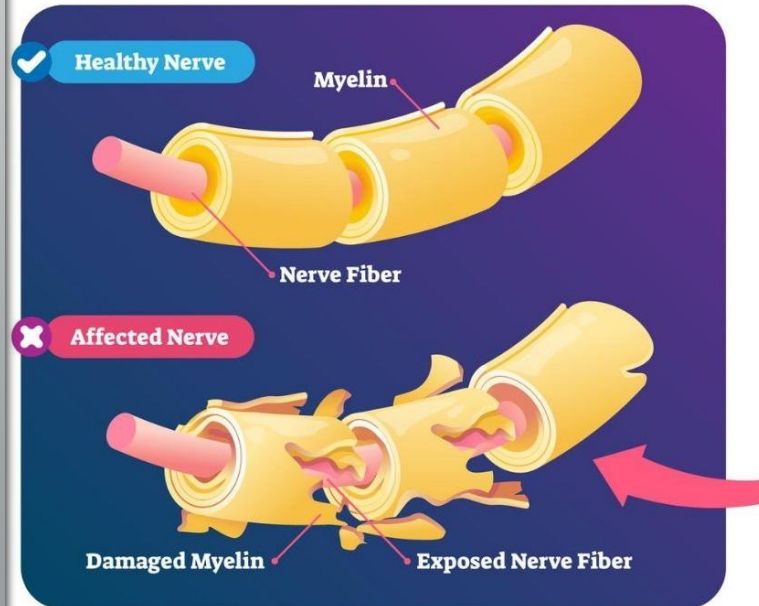


- Myasthenia gravis (MG) is the most common acquired disorder of neuromuscular transmission.
- It occurs due to the production of pathogenic autoantibodies that bind to components of the neuromuscular junction, the most common being the acetylcholinesterase receptor (AChR).
- The incidence is estimated at 0.3 to 2.8 per 100,000 and the worldwide prevalence at 700,000.
- In 1934, cholinesterase inhibition was demonstrated as the first effective treatment for MG.
- A vital capacity (VC) of 15 to 20 mL/kg or a maximal inspiratory pressure (MIP) less negative than  $-25$  to  $-30$  cm  $H_2O$  is often cited as a cut-off for considering intubation in patients with myasthenia gravis.



# Guillain-Barré

## GUILLAIN BARRE SYNDROME



- Guillain-Barré syndrome consists of a group of neuropathic conditions characterized by progressive weakness and diminished or absent myotatic reflexes.
- The estimated annual incidence in the United States is 1.65 to 1.79 per 100,000 persons.
- Guillain-Barré syndrome is believed to result from an aberrant immune response that attacks nerve tissue.
- This response may be triggered by surgery, immunizations, or infections.
- The most common form of the disease, acute inflammatory demyelinating polyradiculoneuropathy, presents as progressive motor weakness, usually beginning in the legs and advancing proximally.
- Symptoms typically peak within four weeks, then plateau before resolving.
- More than one-half of patients experience severe pain, and about two-thirds have autonomic symptoms, such as cardiac arrhythmias, blood pressure instability, or urinary retention.
- Advancing symptoms may compromise respiration and vital functions.
- Diagnosis is based on clinical features, cerebrospinal fluid testing, and nerve conduction studies. Cerebrospinal fluid testing shows increased protein levels but a normal white blood cell count. Nerve conduction studies show a slowing, or possible blockage, of conduction.





# Spinal muscular atrophy



- The term spinal muscular atrophy (SMA) refers to a group of genetic disorders all characterized by degeneration of anterior horn cells and resultant muscle atrophy and weakness.
- The most common SMA, accounting for over 95% of cases, is an autosomal recessive disorder that results from a homozygous deletion or mutation
- In a large, multi-ethnic study to test the feasibility of high-throughput genetic testing for SMA carriers, the overall carrier frequency was one in 54 with an incidence of 1 in 11,000.
- The severity of SMA is highly variable and the clinical features can be classified into four main phenotypes based on age of onset and maximum motor function achieved.
- There is no cure for SMA
- Understanding of the molecular genetics of SMA has led to the development of pre-clinical models and numerous potential therapeutic approaches. There is great excitement in the SMA field as these therapeutic approaches have recently entered early phase clinical trials.
- Paired with the excitement of an active therapeutic pipeline in SMA has been a focus upon understanding the natural history of this disorder as well as early diagnosis and clinical intervention. This has led to the development of clinical standards of care.
- The natural history of the most severe form of spinal muscular atrophy (type 1) has been the subject of particular attention and is characterized by a rapid loss of motor and respiratory function in the first year of life.



# Chronic inflammatory demyelinating polyneuropathy (CIDP)

## **SIDEBAR.** Common Manifestations of CIDP<sup>1,28</sup>

- › Gradually worsening paresthesia and numbness
- › Muscle weakness in legs and arms
- › Areflexia without wasting
- › Preferential loss of vibration or joint position sense
- › Foot drop and difficulty getting out of a chair
- › Difficulty with fine finger control
- › Sensory ataxia
- › Fatigue



# Summary

- Understanding how to match pulmonary function testing to disease condition is very important
- Utilizing PFT test can determine survivability
- Bedside testing is very important in the population
- You can make a difference!



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