# Pulmonary care in SMA: what the spine surgeon should know

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# Disclosures

- Cure SMA – Paid Medical Director
- AveXis - Advisory Committee Member
- Biogen Idec – Advisory Committee Member
- IONIS Pharmaceuticals – Advisory Committee Member
- HHS/HRSA/Maternal Child Health Bureau – Pediatric Pulmonary Center Training Grant

# Learning Objectives

Participants will:

1. Identify the effects of neuromuscular weakness on respiratory pathophysiology and the resulting respiratory complications.
2. Describe management strategies that optimize respiratory function.
3. Consider the impact of gene modifying therapy on SMA.

# Standard of Care Guidelines SMA

Special Issue Article

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## Consensus Statement for Standard of Care in Spinal Muscular Atrophy

Ching H. Wang, MD, PhD, Richard S. Finkel, MD, Enrico S. Bertini, MD, Mary Schroth, MD, Anita Simonds, MD, Brenda Wong, MD, Annie Aloysius, MRCSLT, HPC, Leslie Morrison, MD, Marion Main, MCSP, MA, Thomas O. Crawford, MD, Anthony Trela, BS, and Participants of the International Conference on SMA Standard of Care

Encompasses:

- Diagnosis
- Respiratory Care
- GI and Nutrition
- Musculoskeletal
- Palliative Care

Wang C et al, J. Child Neurol 2007; 22:1027.

# Spinal Muscular Atrophy

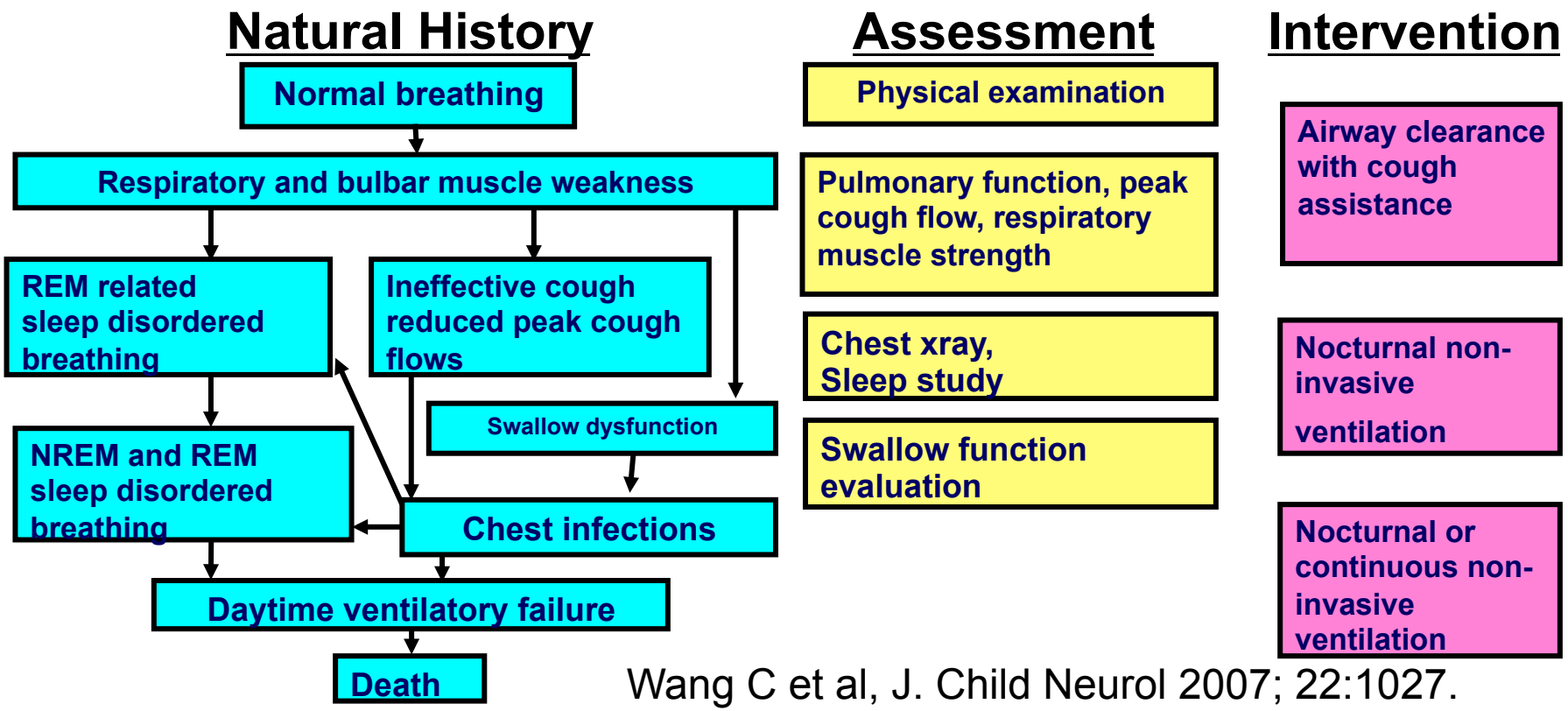
- Multi-organ involvement
  - Musculoskeletal
  - Respiratory
  - GI and nutrition
  - Bone health
  - Autonomic
  - Mental health
  - Cardiac

- It takes a village…

# Neuromuscular Disorders

- Cause of death is usually respiratory failure.

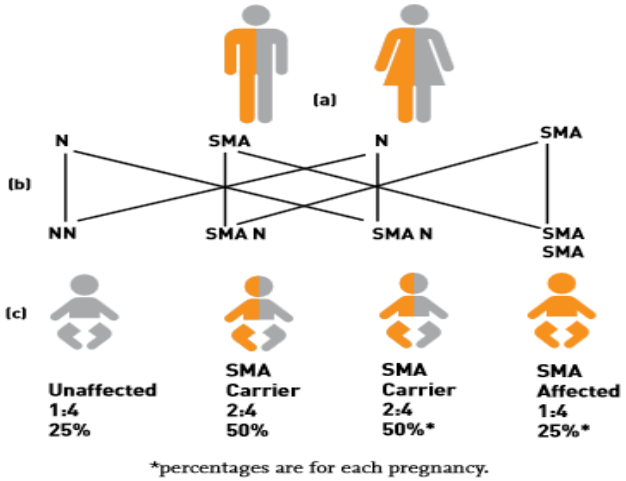
# SMA Pulmonary Natural History



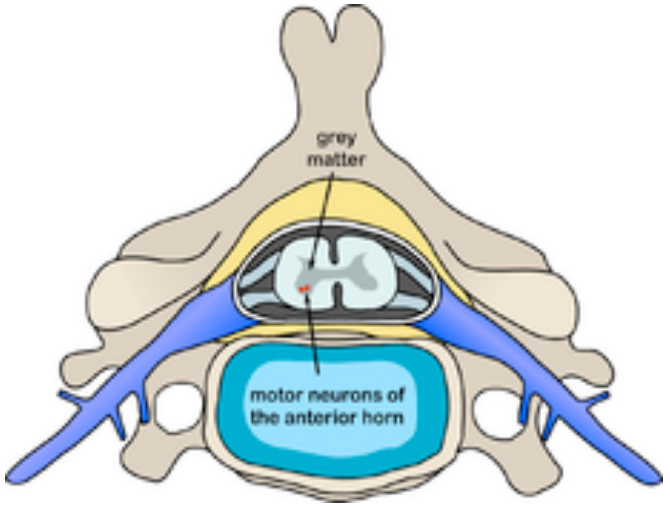

Wang C et al, J. Child Neurol 2007; 22:1027.

# Spinal Muscular Atrophy

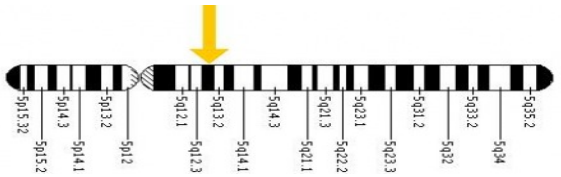
- Progressive **autosomal recessive** genetic disorder
    - affects the motor neurons of the anterior horn cells.




*percentages are for each pregnancy.



# SMA Genetics

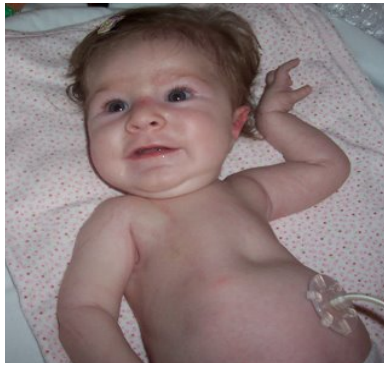



- Carrier rate: 1 in 50
- Incidence estimate: 1/6,000-1/10,000 live births
- Diagnose by gene mutation testing
  -Chromosome 5q (>95%)
    - Homozygous deletion of SMN1 exon 7 and/or exon 8 OR
    - Gene conversion of SMN1 to SMN2-like
  -Remaining 5% have point mutation


- Most common lethal genetic disease of children under 2 yo

# SMA Clinical Manifestations

- Symmetric muscle weakness
- Wasting of voluntary muscles
  - Proximal muscles weaker than distal muscles
  - Legs weaker than arms
  - Tongue fasciculations
  - Absent deep tendon reflexes
  - Weak intercostal muscles in SMA type I and II
- Normal intellect and sensation
- “Bright-eyed hypotonic baby”



# Clinical Classification of SMA

| SMA TYPE | Incidence | Age of Onset | Motor Milestones | Ave Age of Death (limited interventions) |
|---|---|---|---|---|
| I | 50-60% | < 6 months | Non sitter | < 2years |
| II | 25% | < 18 months | Sitter | 2nd - 3rd decade |
| III | 10% | > 18 months | Stander/walker | Normal life expectancy |
| IV | 5% | Adolescent or Adult onset | Retain walking, muscle pain | Normal life expectancy |

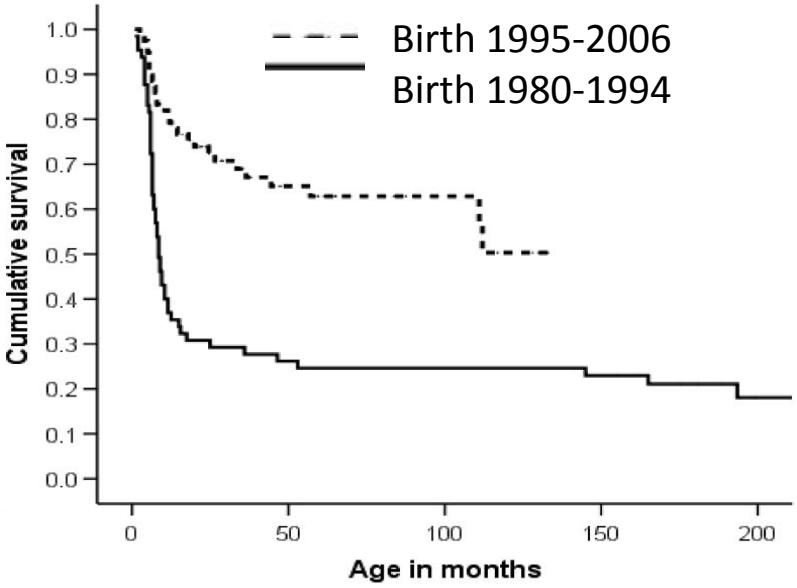
# Changing Natural History of SMA Type I

- Comparison of children with SMA type I born between:
  - 1980-1994 (n=65)
  - 1995-2006 (n=78)
- Subjects identified using the Indiana University International SMA Patient Registry
- Surveyed by mail with follow up questions.

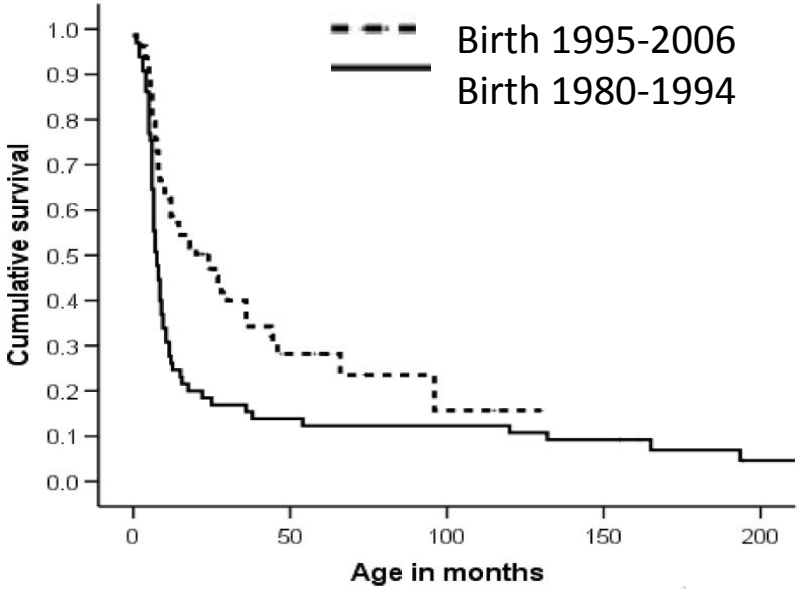
Oskoui M et al, Neurol 2007; 69:1931.

# Kaplan–Meier survival plots of Spinal Muscular Atrophy type 1

**Event death**




**Events death or ventilation >16 hours**




Oskoui M et al, Neurol 2007; 69:1931.

# SMA Gene

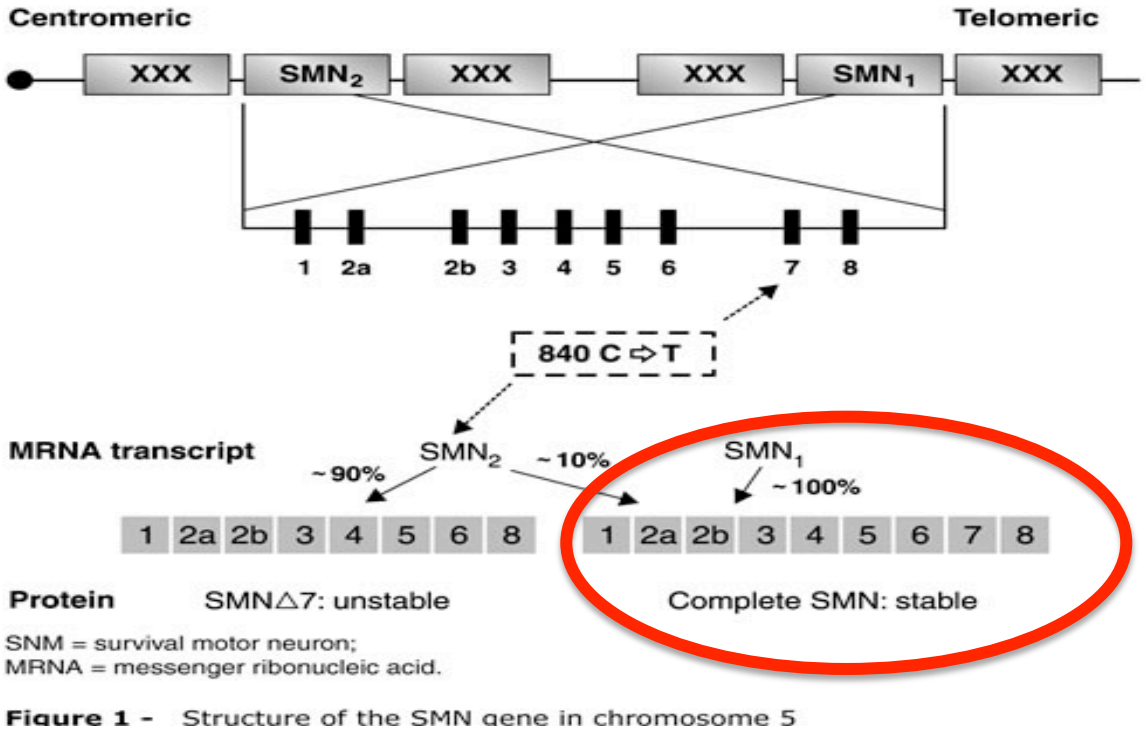



**Figure 1 -** Structure of the SMN gene in chromosome 5

Baioni MTC, et al, J Pediatr (Rio J). 2010;86(4):261-270

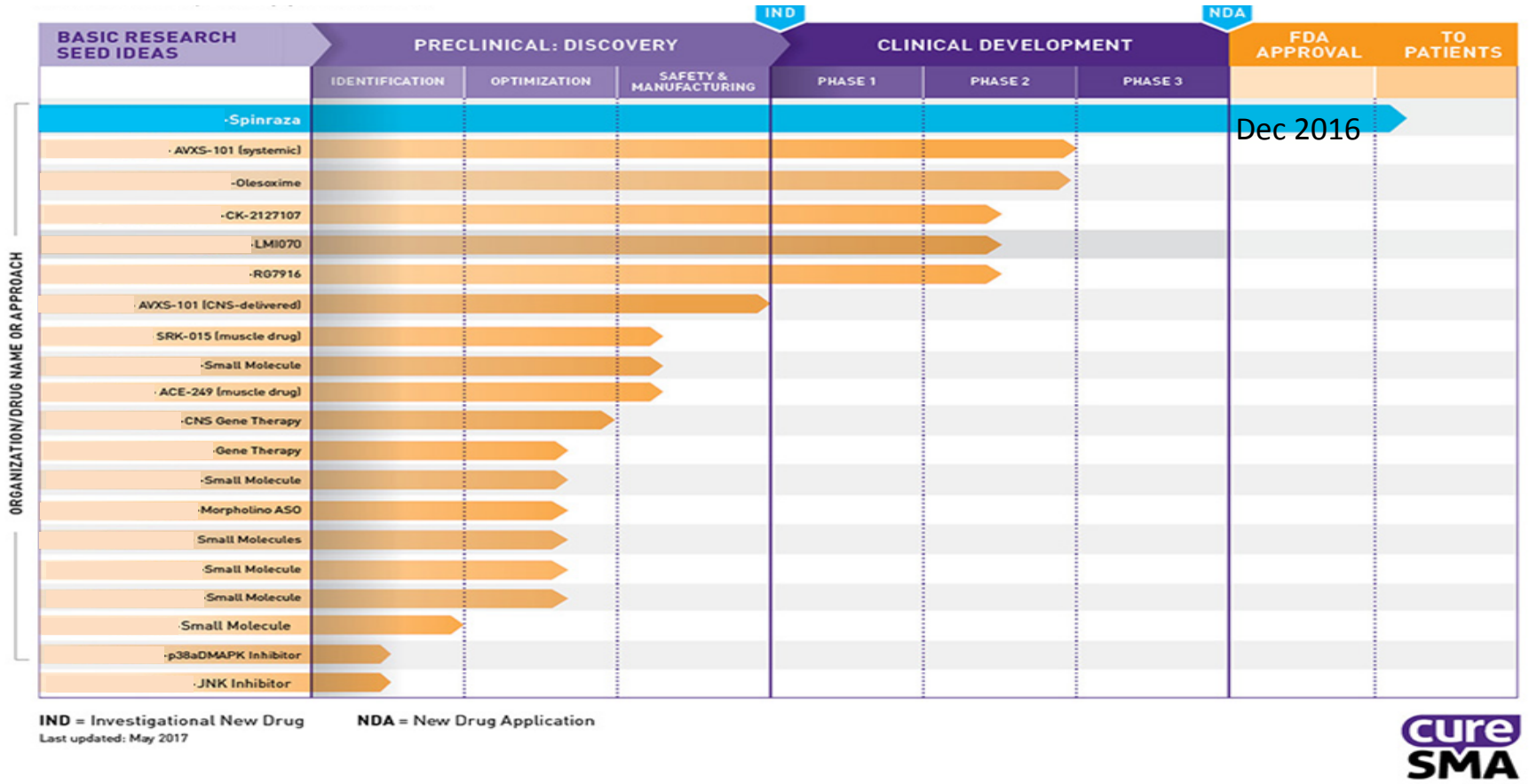
# Phenotype/Genotype (cont.)

SMN2 gene copy number varies in the population and modifies disease severity

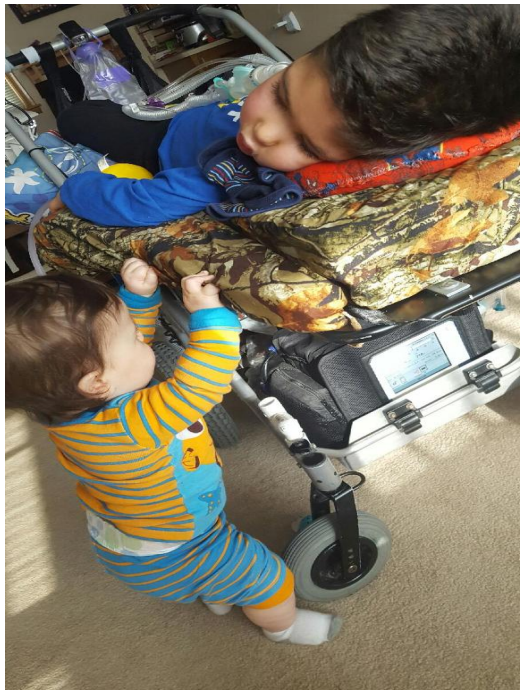
| | % SMA type | | |
|---|---|---|---|
| *SMN 2* copy # | SMA 1 | SMA 2 | SMA 3 |
| 1 | 7 | 0 | 0 |
| 2 | 73 | 11 | 4 |
| 3 | 20 | 82 | 51 |
| 4 | 0 | 7 | 45 |
| Total | 100% | 100% | 100% |

Courtesy of Thomas Crawford MD, Presentation at Cure SMA Annual Conf 2015

# 2017 SMA Drug Discovery Pipeline



# Gene Modified SMA

# Respiratory Management

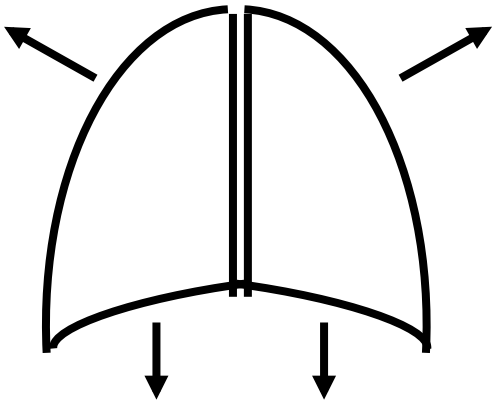
# Complications of Respiratory Muscle Weakness in SMA

1. Impaired cough
   - Poor clearance of lower airway secretions
2. Hypoventilation during sleep
   - hypercarbia
   - hypoxemia
3. Recurrent infections that contribute to muscle weakness.
4. Chest wall and lung underdevelopment in SMA type I and II

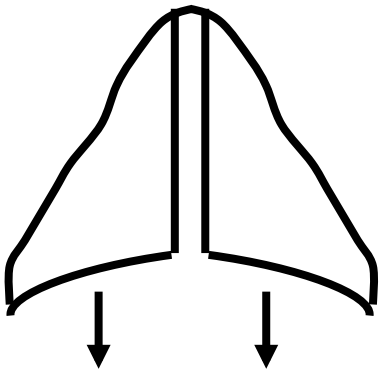
Wang C et al, J Child Neurol 2007; 22:1027.

# Chest Wall Changes

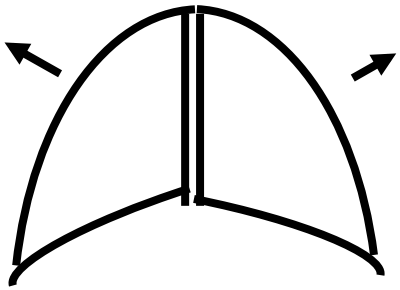
**Normal**



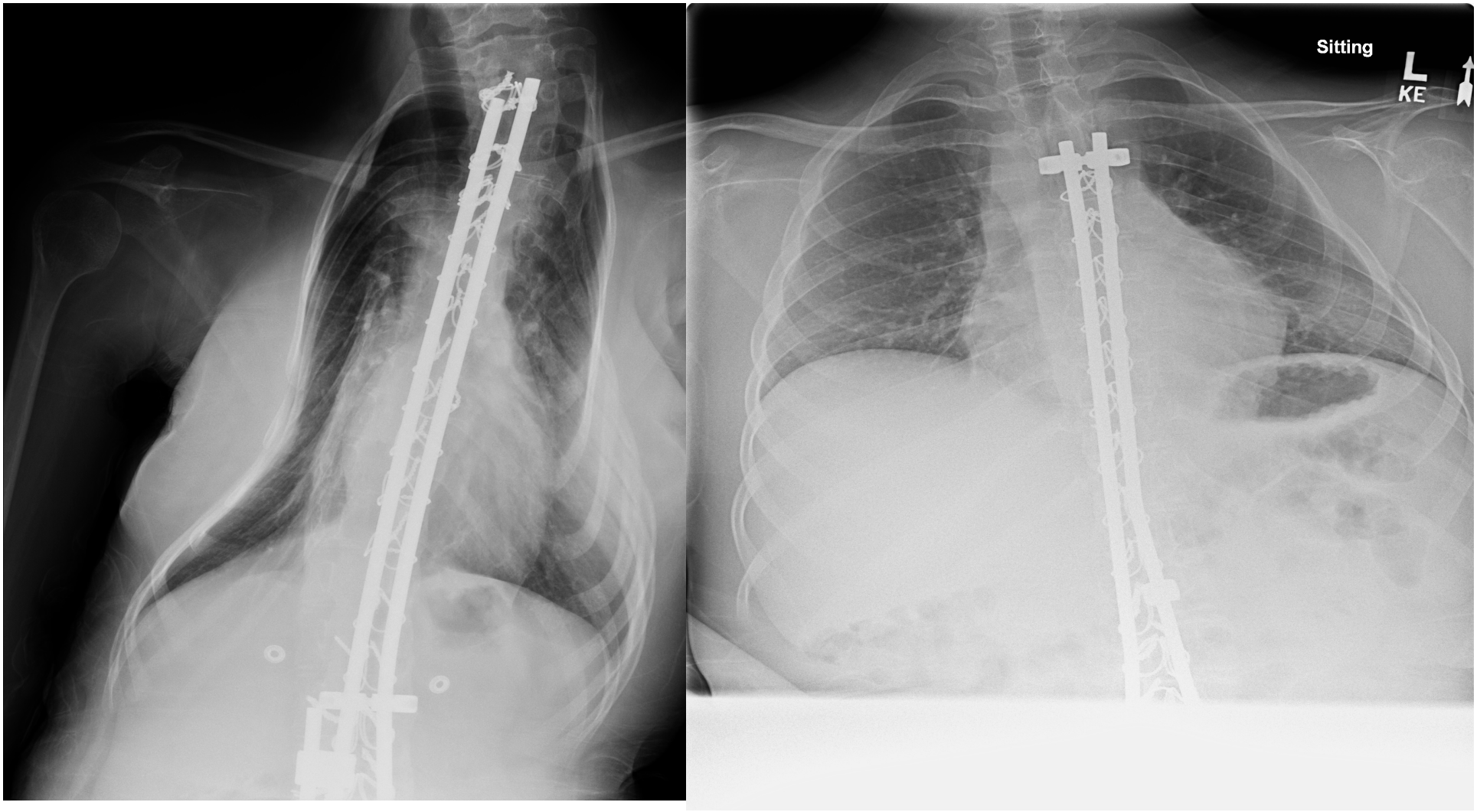
**SMA**



**DMD**



Schroth, Pediatrics, 2009; 123 Suppl 4, S245-9.


Sitting
L
KE

# NMD Lung Function Loss

- **VIRAL RESPIRATORY INFECTIONS**
  - Rhinovirus RSV Parainfluenza Influenza Etc…
  - Transient muscle function weakness
    Mier-Jedrzeiowicz A et al, Respiratory muscle weakness during upper respiratory tract infections, ARRD 1988 Jul;138(1):5.

- IMPACT:
  - Increased muscle weakness
  - Copious airway secretions
  - More difficulty breathing
  - Risk for respi

# Perioperative Care

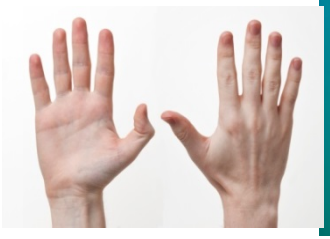
- Respiratory Support
- Nutrition

# Breathing Basics

- Secretion mobilization
- Cough Augmentation
- Respiratory support

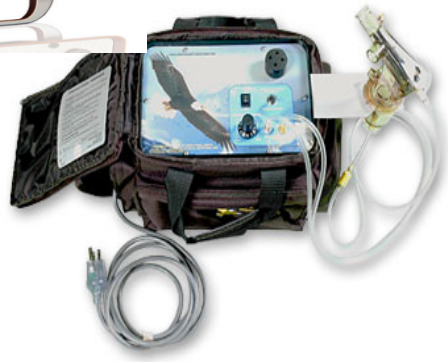
# Secretion Mobilization

- Manual Chest Physiotherapy or Mechanical Percussion

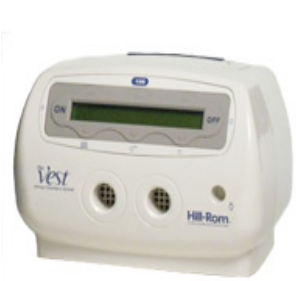


- Postural Drainage

# Other Techniques

**Intrapulmonary Percussive Ventilation**




**High Frequency Chest Wall Oscillation**

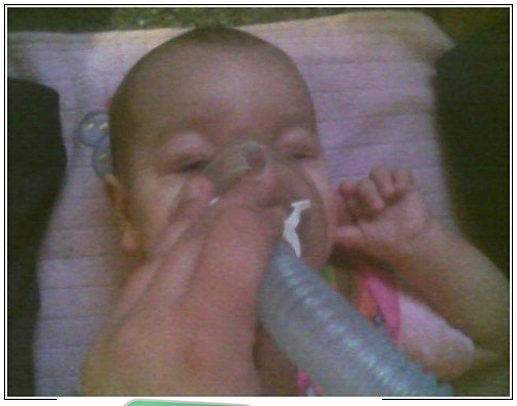
# Cough Mechanism

3 Phases of a cough

1. Inspiratory phase
2. Closure of vocal cords/contraction of expiratory muscles
3. Opening of the vocal cords

# Mechanical Insufflation-Exsufflation: Cough Machines

Respironics
Cough Assist™ CA-3000

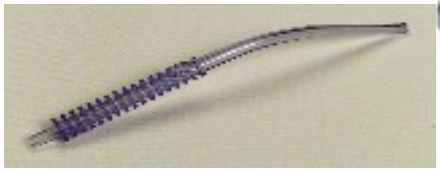


Respironics
Cough Assist™ T70

Hill-Rom Vital Cough™

# Cough Machine

- SETTINGS to use by mask, mouth piece, tracheostomy tube or endotracheal tube.
  - INSPIRATORY
    - Start at +25-30, increase to +40 cm $H_2O$ for 1-2 sec.
  - EXPIRATORY
    - Start at –25-30, increase to -40 cm $H_2O$ for 1-2 sec.
  - PAUSE TIME
    - 1-2 sec.
  - Perform 4 sets of 5 breaths

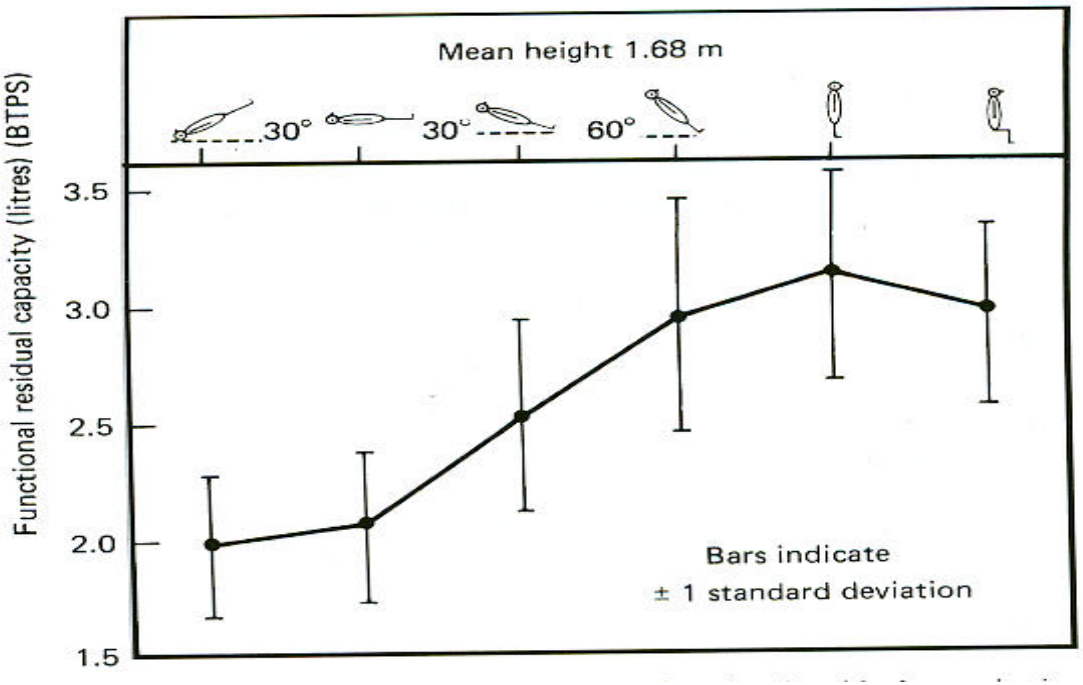


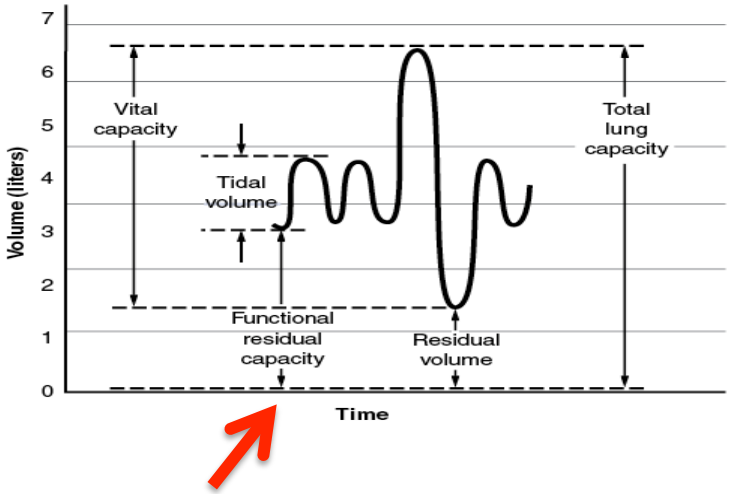
# Pulse Oximetry

- Use to guide airway clearance therapy
- Acutely decreased oximetry (< 95% while AWAKE)
  - suggests increased secretions, mucus plugging, or atelectasis.
  - may be the first sign of respiratory compromise.
- < 95% while ASLEEP
  - suggests hypoventilation or mucus plugging.


**OXYGEN IS A LAST RESORT AFTER ALL OTHER INTERVENTIONS ARE OPTIMIZED!**

# FRC Relative to Position




From Nunn's Applied Respiratory Physiology, 2000

# Respiratory Support Options

- Used during sleep or at least 6 hours per day
- Non-invasive ventilation
  - Bilevel positive airway pressure
  - Mechanical ventilation
- Invasive ventilation
  - Tracheotomy with Mechanical ventilation

# Chronic Respiratory Failure: Bilevel Positive Airway Pressure Effects

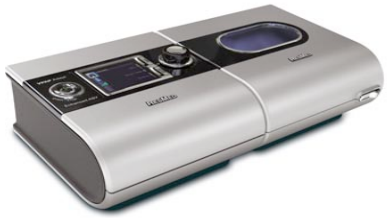
- Sustained reduction of daytime PaCO2
  - 3 Theories for NIV effect:
    - Rests chronically fatigued respiratory muscles
    - Reverses micro-atelectasis
    - Alters the CO2 “set point”

Mehta and Hill, Am J Respir Crit Care Med 2001; 163:540

# Positive Pressure Ventilation Devices

1. Bilevel positive airway pressure devices

   Non- invasive only

nec

tila


**CPAP is NOT INDICATED for Neuromuscular hypoventilation**

## Non Invasive Bilevel Positive Airway Pressure

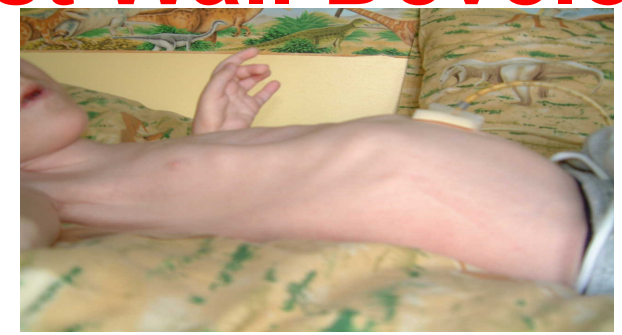
- Goals:
  - Ventilation
  - Decrease work of breathing – rest respiratory muscles
    - » Decrease belly breathing
    - » Normalize heart rate during sleep
  - Improve chest wall expansion

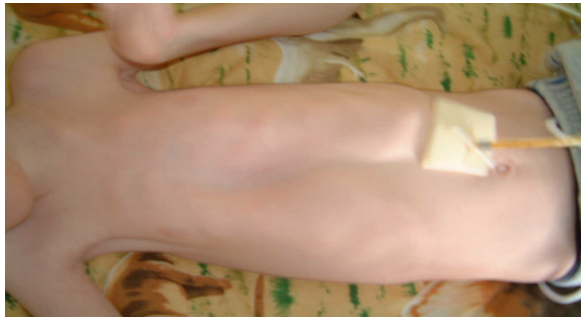
# Indications for Positive Pressure Ventilation

- Sleep study:
  - Hypoventilation ($\Downarrow$ SpO2, $\Uparrow$ pCO2)
  - Obstructive sleep apnea
- Specific to NMD
  - Respiratory failure during a viral illness
  - Recurrent pneumonia or atelectasis
  - Post-operative care

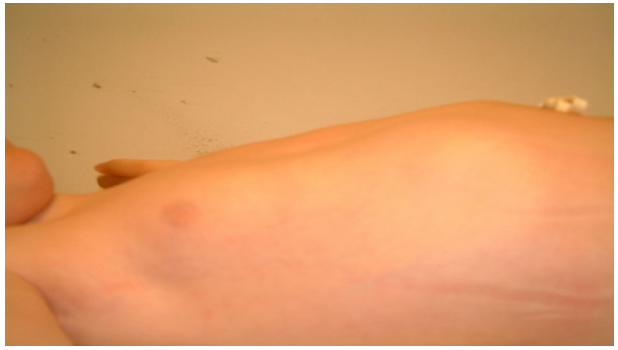
# Chest Wall Development After NIV

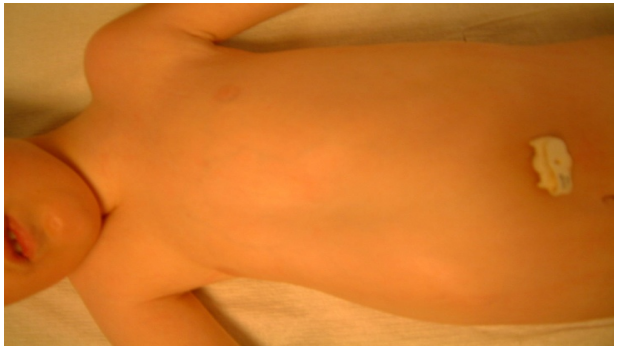
6 mths





18 mths





Courtesy of A. Simonds, Royal Brompton Hospital, UK

# Nasal Masks

## Respironics Wisp Pediatrics

## Infant to 2 yo:

- Respironics Wisp Pediatrics
- AG Industries Nonny

## Over 2 years old:

- ResMed Pixi
- Sleepnet MiniMe 2
- Respironics Wisp
- Fisher & Paykel Eson
- Fisher & Paykel Zest

## AG Industries Nonny, Size Small Child, AG-PEDKIT-S

# Invasive Ventilation

- Tracheostomy placement
  - Not an acute intervention
  - Involve primary medical team in decision making
- Indications
  - 24 hour per day NIV dependent
  - Frequent cyanotic episodes or respiratory instability on NIV
  - NIV intolerance
  - Failure to extubate
  - Patient preference

Wang C et al. J. Child Neurol 2007; 22:1027.

# Positive Pressure Ventilation

- Goals during **sleep**:
  - Respiratory muscle rest
  - Synchronization
  - Chest wall expansion

- Recommended modes:
  - **PC (Pressure control)** guaranteed inspiratory time with back up rate
  - ST (spontaneous timed) with back up rate
  - PC-AVAPS (average volume assured pressure support) targeted tidal volume within IPAP range
    - IPAPmin must be high enough to support ventilation
- Backup respiratory rate required

## Non Invasive Bilevel Positive Airway Pressure

- IPAP: 14-20 cm of $H_20$
- EPAP: 4-6 cm of $H_20$
- Respiratory Rate: high enough to capture breathing efforts and rest during sleep.
- Inspiratory Time: Longer time preferred to maximize inflation 1.2 seconds
- Rise time: time between exhalation and rise to peak inspiratory pressure (IPAP)

# GI and Nutrition Complications

- Dysphagia
  - Aspiration
  - Weight loss
- Gastroesophageal reflux
- Gastroparesis
- Constipation
  - Decreased  appetite
  - NIV intolerance
- Poor weight gain
- Obesity

# GI and Nutrition Complications (cont.)

- Large insensible fluid losses
  - Perspiration
  - Suctioning oral/nasal secretions
  - Hospital I&Os are never balanced
  - 1.2x maintenance

# GI and Nutrition Complications SMA Specifically

- Abnormal fatty acid oxidation
  - Abnormal dicarboxylic aciduria in response to fasting
  - Avoid high fat diet (Max: 20% of calories)
  - Ketosis and ketonuria with fasting/dehydration
  - Avoid fasting in weakest group: anyone with tube feeds

Tein et al. Fatty Acid Oxidation Abnormalities in Childhood-Onset Spinal Muscular Atrophy: Primary or Secondary Defect(s)? Pediatr Neurol 1995;12:21-30.

# Respiratory Therapy NMD Protocol

- Scoring system to guide frequency of airway clearance and time off ventilation if not 24 hour dependent
- Aggressive airway clearance:
  - Cough assist machine while intubated
  - Secretion mobilization techniques
  - Postural drainage if not ETT intubated

# Extubation

Extubate when the patient is:

1. Afebrile
2. **Not requiring supplemental O2**
3. CXR is without atelectasis or infiltrates
4. Minimal respiratory depressants
5. Airway suctioning is 1 time/hour or less
6. Motor strength and alertness approaching baseline

# Extubation (cont.)

- Extubate from reasonable settings:
  - respiratory rate similar to the optimal baseline positive pressure device respiratory rate
  - pressures that approximate BiPAP IPAP (15-20) and EPAP (3-6)
  - room air
  - Wean to use during sleep
- Avoid low ventilator rates through ET tube especially during sleep
  ⇒ atelectasis/fatigue.
- Continue aggressive airway clearance post extubation.
  - Increased airway secretions for 24 hours post extubation

# Other Complications of NMD

- Osteopenia – poor bone health
- Scoliosis
- Joint contractures
- Rapid fatigue
- Pain
- Depression

# UW Pediatric Neuromuscular Disorder Program

- Respiratory Care
  - Physician/Nurse practitioner
  - Respiratory care practitioners
- Neurology
  - Physician/Nurse practitioner
- Care coordination
  - Clinic coordinator
  - Case Manager
- Palliative Care
  - Physician/Nurse practitioner
- Genetic Counselor
- Nutritionist
- Social Worker

- Orthopedic and Rehabilitation Medicine Services
  - Physician/Nurse practitioner
  - Physical Therapist
  - Occupational Therapist
  - Speech Therapist
  - Orthotist
  - Vocational Rehabilitation Coordinator
- Cardiology
  - Physicians
  - Nurse Practitioner

# Summary

- The respiratory complications of neuromuscular disease include:
  - Hypoventilation during sleep and with disease progression while awake
  - Compromised airway secretion clearance
- Supplemental oxygen is not the answer
- Use positive pressure ventilation at settings to ventilate and rest the patient during sleep.

# Summary

- Perioperative care includes optimization of pulmonary status and nutrition status.
  - Pulmonary consultation
  - Nutrition consultation

# Summary

- The natural history of many neuromuscular diseases are evolving with longer survival and improved care options.
- Gene modifying therapy is creating another form of SMA.
- Interdisciplinary management is essential.

# Additional Information

- Cure SMA website: www.curesma.org
- SMA Foundation website: www.smafoundation.org
- Muscular Dystrophy Association website: www.mdausa.org

# Questions/ Comments/ Discussion