Management of Respiratory Problems in Pediatric NMDs

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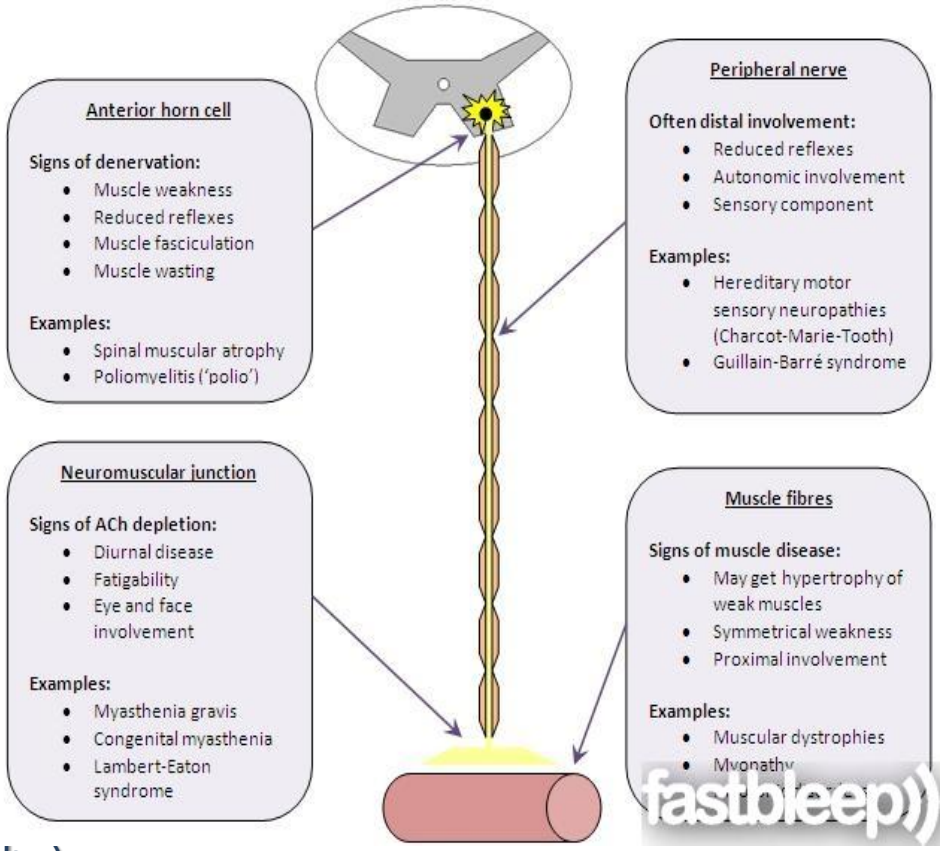
Neuromuscular diseases (NMDs)

- Includes diseases of
  - the Ant. Horn cells
  - the Peripheral nerves
  - the Neuromuscular junctions
  - the Muscles

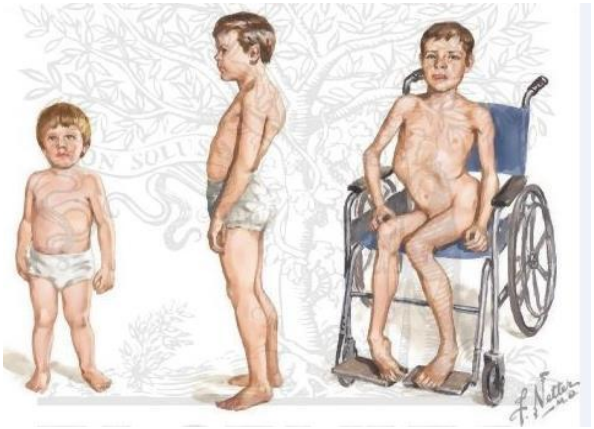
- 2 most common pediatric NMDs that exemplify the important principles of respiratory management

  1) DMD (Duchenne Muscular Dystrophy)

  2) SMA (Spinal Muscular Atrophy)



Duchenne Muscular Dystrophy (DMD)



- M/C neuromuscular condition in childhood
- Incidence (1:3,500 male births)

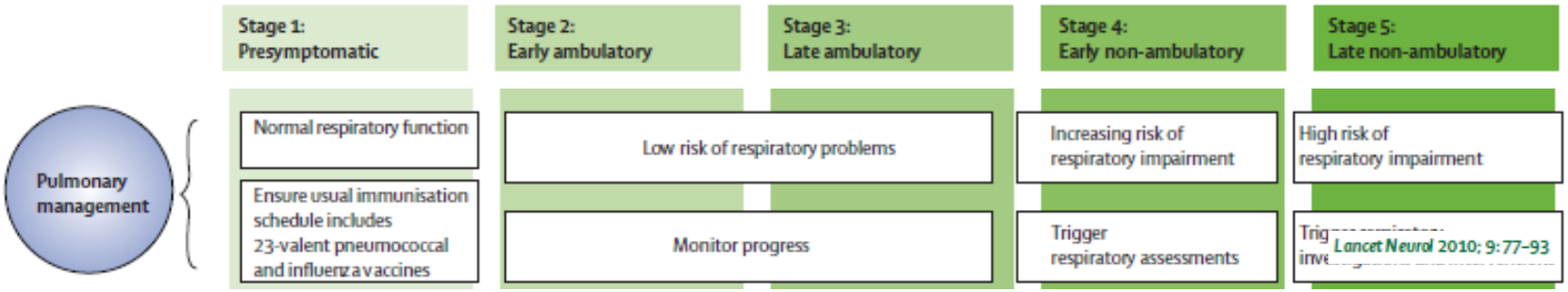
- X- linked recessive (Xp21 gene loci)
- Absence or defect of dystrophin protein, resulting in progressive weakness & wasting of all the striated muscles

- Identified by 5-6 years of age
- Loss of ambulation in early teen years

- Premature death due to respiratory & cardiac complication
- Implementation of interdisciplinary care

  → Now has a life expectancy into the forth decades

- Ambulatory DMD normally have few respiratory difficulties



- Progressive risk of respiratory complications over time
  - → Ineffective cough
  - → Nocturnal hypoventilation
  - → Sleep disordered breathing
  - → Daytime respiratory failure

Spinal Muscular Atrophy (SMA)

- Mostly disorders with childhood onset, usually by AR inheritance
- By deletion of SMN gene on chromosome 5_q13

- Degeneration of spinal cord motor neuron
  → progressive muscular atrophy, weakness, respiratory insufficiency

- Presents 2 forms during infancy
  (SMA type 1 & 2)

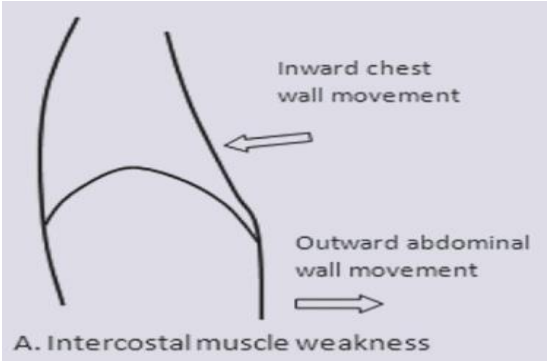
- Association between onset age
  & disease severity

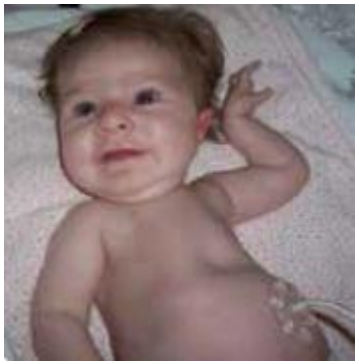
Table 46-1 Spinal Muscular Atrophy

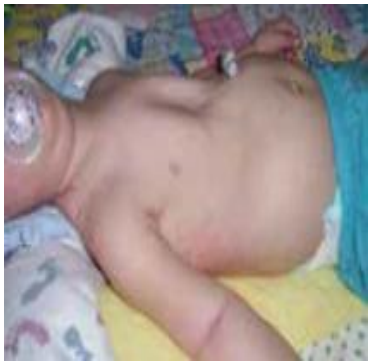
Type	Synonyms	Disease onset	Natural History
SMA I	Werdnig Hoffman Acute infantile	Before 6 months of age	Unable to sit independently Poor survival
SMA II	Werdnig Hoffman Chronic infantile	Before 18 months of age	Sits independently No independently ambulation Over 50% Survive to mid-20s
SMA III	Kugelberg-Welander Chronic juvenile	After 18 months of age	Ambulates independently Normal survival
SMA IV	Adult onset	Mean onset in mid-30s	Normal survival

Spinal Muscular Atrophy (SMA)

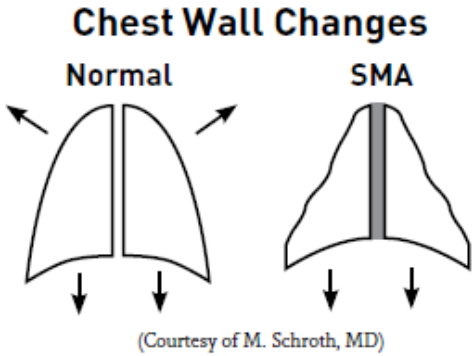
- Intercostal m. weakness with relative sparing of the diaphgram
- Rib cages fail to expand outward while diaphragm pulls the rib cage downwards
  - Paradoxical breathing pattern
  - Bell shaped chest
  - Pectus Excavatum







→ Requires special attention for NL lung development

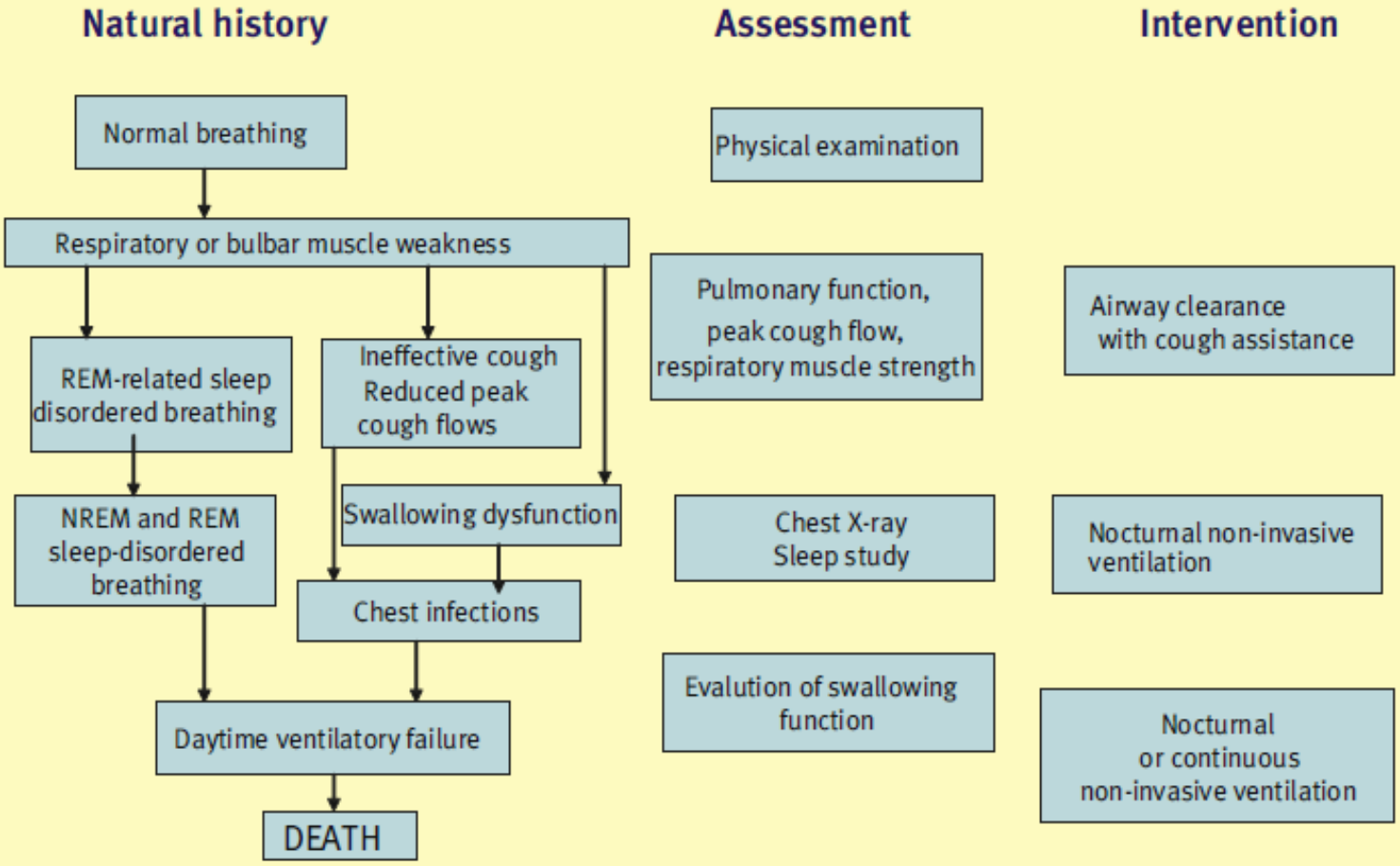


Spinal Muscular Atrophy (SMA)

- Pulmonary disease is the major cause of morbidity & mortality in SMA type 1,2

- Main respiratory problems in pediatric SMA
  - Impaired cough resulting in poor clearance of secretions
  - Recurrent infections that exacerbate muscle weakness
  - Hypoventilation during sleep
  - Underdevelopment of chest wall & lung

Pulmonary natural history, assessment and intervention



Respiratory Function Assessment
; patient symptoms

- While patients walk,
  - Exertional dyspnea
- For W/C users,
  - Symptoms may be minimal
  - ↑rate, ↓depth, irregularity of breathing
- Symptoms of nocturnal hypoventilation
  - Nocturnal arousals & frequent repositioning
  - Morning headache, daytime sleepiness, fatigue
- Symptoms may be poorly indicative of sleep breathing difficulties.

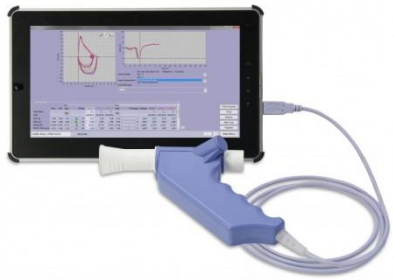
Respiratory Function Assessment ; PFT

- Maximum Inspiratory Pressure & Expiratory Pressure (MIP & MEP)
  - Best correlated with inspiratory & expiratory muscle strength

(Figure 4) Measuring Respiratory Muscular Strength

- Vital Capacity (VC)
  - simple, easy to measure
  - objective, reproducible

- Supine VC
  - most important indicator of ventilatory dysfunction (hypoventilation is often worst during sleep)



Respiratory Function Assessment ; PFT

- Maximum insufflations capacity (MIC)

  - Maximum volume of air stacked within the patient's lungs beyond spontaneous vital capacity

  - by giving the patients largest volume of air that can be held with closed glottis

  - by teaching patient to stack volumes delivered from manual resuscitator or volume-cycled ventilator

(Figure 5) How to Measure the Maximum Insufflation Capacity

Respiratory Function Assessment ; PFT

- Peak Cough Flow (PCF)

  - important measures of the capacity for mucociliary clearance

  - 270 L/min as the acceptable level of flow*

- *160 L/min*

  - minimum needed to eliminate airway secretion

  - Best indicator for
    <u>tracheostomy tube removal</u>
    (*irrespective of remaining pulmonary function)*

Respiratory Function Assessment
; Gas exchange monitoring

- ABGA (Arterial Blood Gas Analysis)

  - Unnecessary for stable patients /s intrinsic pulmonary disease

    (25% hyperventilation during procedure: anxiety or pain)

- Noninvasive continuous blood gas monitoring

  - More useful information, particularly during sleep

  - O2 saturation monitor by pulse oxymeter

  - End-tidal CO_2 monitoring
    or transcutaneous CO_2 monitoring

Respiratory Function Assessment
; Sleep Apnea

- Symptomatic patient with normal VC
  unclear pattern of SaO_2
  no apparent CO_2 retention,
  - Loud high-pitched snoring
  - Interrupted breathing
  - Hypersomnolence

  → Sleep disordered breathing suspected

  → Polysomnography & CPAP should be considered

Respiratory Function Assessment

- Serial monitoring of lung function is mandatory
  - Patients should have at least 1 visit early in the course of disease (4-6 yrs age) to obtain baseline PFT
  - Patients should visit for respiratory care twice yearly after W/C bounded, FVC<80%$_{pre,}$ and/or age 12 yrs
  - Individuals requiring assisted airway clearance or mechanical ventilation should visit every 3-6 months or as indicated for routine F/U

- Patients with SMA 1,
  - lung function testing is technically demanding
  - monitoring /c oximetry, capnography is extremely helpful in assessing evolving respiratory m. weakness & resultant hypoventilation

Respiratory Function Assessment

- Objective evaluation at each clinic visit

  → SpO_2, FVC, MIP & MEP, PCF
- Awake CO_2 should be evaluated at least annually /c capnography
- Useful additional measures

  : assisted PCF, maximum insufflation capacity (MIC)

- Annual lab studies for W/C dependents

  : complete blood count, serum bicarbonate concentration, chest radiograph

Basic objectives of Respiratory Management

1) **Maintain lung & chest-wall compliance**
   & Promote lung & chest-wall growth for children

2) **Maximize cough flow**

3) **Maintain normal alveolar ventilation around the clock**

Deep lung insufflation

- Also known as "air stacking" or "breath stacking"
- Inflate and recruit the lung

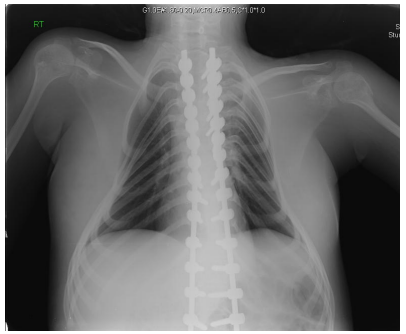
- Inspiratory Pr. applied to airway, hold of the delivered volume by glottic closure, followed by forced expiratory maneuver

- Helps to prevent atelectasis, limit contractures of the thoracic m & maintain chest wall motions

- Indicated when FVC < $70\%_{pre}$

  → instructed to air-stack <u>10-15 times at least 2-3 times/day</u>

Deep lung insufflation



- Infant (SMA type 1,2) cannot air stack or cooperate to receive maximal insufflations
  → paradoxical chest wall movement
  → Noctural NIV to prevent pectus excarvatum & Promote lung growth as well as for ventilatory assistance

- Deep insufflation with concomitant abdominal compression
  by timing the delivery of air to the child's breathing phases

- Children (14-30 months) can cooperative with deep insufflation therapy

Airway Clearance

- Becomes impaired after the patient loses the ability to ambulate
- Critical to prevent atelectasis and pneumonia

- Effective coughing when MEP ≥ 60cmH_2O, absent at 45 ≤ cmH_2O
  when PCF > 270L/min, ineffective at< 160L/min

- 160 < PCF < 270 : can benefit from assisted coughing techniques in case of viral illness when secretion increase

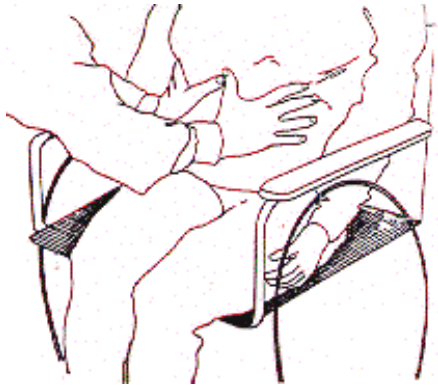
Airway Clearance

- Patients with NMD should be taught airway clearance techniques early and aggressively

- Recommend indications:
  1) Clinical history suggests difficulty in airway clearance
  2) PCF < 270 L/min, and/or MEP <60 cm H_2O
  3) Baseline FVC <40%$_{pre}$ or <1.25L in older teenagers

- Once recommended, 1-2/day as maintenance therapy to improve airway clearance & reduce atelectasis

Airway Clearance



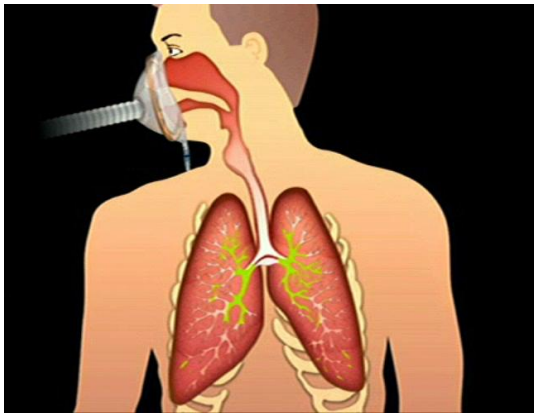
- *Manual assisted coughing*

  - Inspiratory assistance followed by augmentation of the forced expiratory effort

  - Inspiratory assist by the use of glossopharygeal breathing (GPB), air stacking or mechanical ventilator

  - Forced exhalation by pushing on the upper abdomen or chest wall in synchrony with the subject's own cough effort

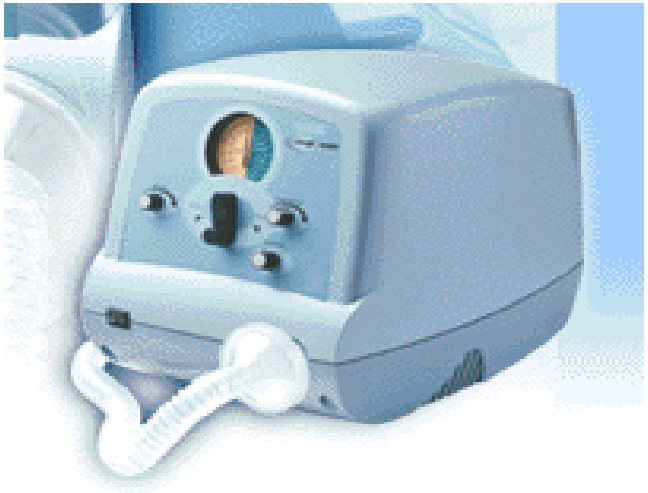
Airway Clearance



- *Mechanical insufflator-Exsufflator (MI-E)*

  - stimulate cough by proving a positive Pr. followed by negative Pr.
  - superior peak cough expiratory flow rates than by breath stacking or manual cough assistance
  - preventing hospitalization or need for tracheostomy /c PCF around 160L/min, especially when scoliosis prevented optimal use of manual assisted cough

- Efficacy of MI-E
  - Airway mucus elimination
  - Improvement of VC & pulmonary flow rates
  - Normalization of SpO2



Cough Assist™

Cough Assist E70

CNS (Cough & Suction)

Comfort Cough™

Support of nocturnal ventilation

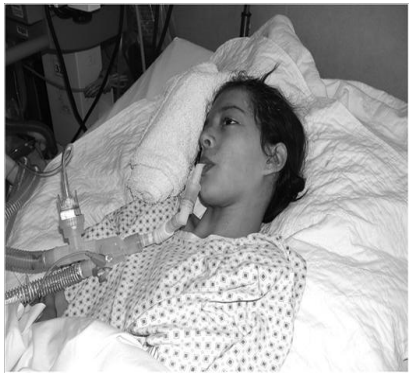
- Nocturnal hypoventilation occurs after the loss of an effective cough

- Awareness of the hypoventilation symptoms
  - Headaches all the time or in the morning
  - Sleepiness for no reason
  - Trouble sleeping, frequent wake-ups, nightmares

- Noninvasive intermittent positive pressure ventilation (NIV)
  - Inspiratory muscle aids
  - Major Tx. of respiratory failure of pediatric NMDs since subsequent development of children's masks

Support of nocturnal ventilation

- Various NIV interfaces for children



Support of nocturnal ventilation

- Little consensus regarding when to start NIV

- Recommended indications:

  Signs or symptoms of hypoventilation plus one of the following

  1) $PaCO_2 \geq 45$ mm Hg
  2) Nocturnal $SpO_2 < 88\%$ for 5 consecutive minutes
  3) MIP <60cmH_2O or FVC <50% of predicted

- Optimally, use of lung volume recruitment and assisted cough techniques should always precede initiation of non-invasive ventilation

Support of nocturnal ventilation

- Nocturnal NIV in NMD
  - Improves daytime gas exchange, slower decline in lung function
  - Improves daytime sleepiness
  - Improves well-being & independence
  - Positive effects on lung & chest wall growth
  - Improves survival

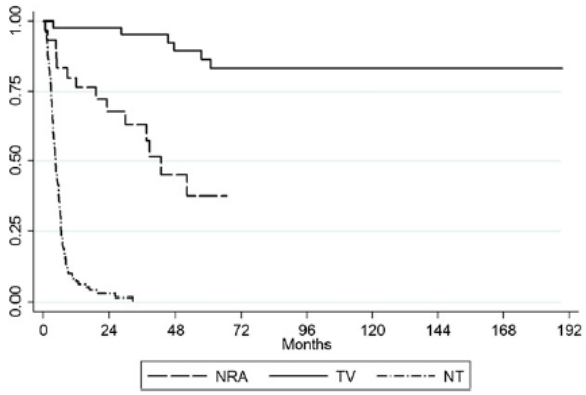


FIGURE 1
Kaplan-Meier estimates of survival in the 3 groups. The cumulative probability of survival was greater for continuous NRA and TV groups, with a lower survival probability at ages 24 and 48 months in the NRA group.

Pediatrics 2013;131:e1509–e1514

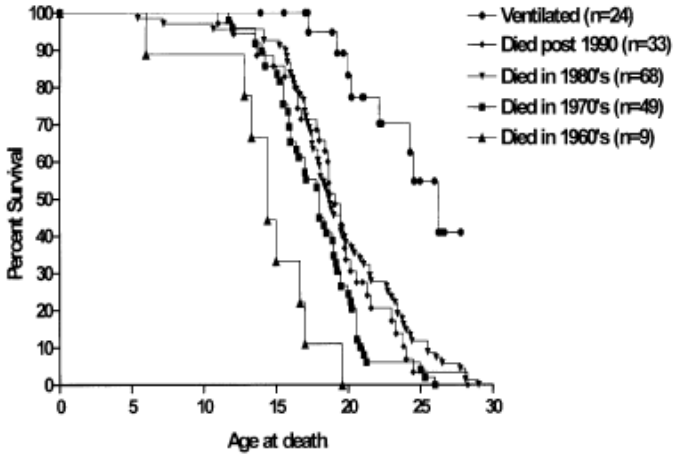


Fig. 2. Survival curves (Kaplan Meier) showing percentage survival of ventilated versus non-ventilated patients 1967–2002. (Includes live patients

M. Eagle et al. / Neuromuscular Disorders 12 (2002) 926–929

Support of nocturnal ventilation

- Relative contraindications for long-term NIV

1. Lack of cooperation or use of heavy sedation or narcotics
2. Need for high levels of supplemental oxygen therapy
3. SpO_2 can not be maintained above 94% despite noninvasive IPPV and optimal use of assisted coughing techniques when needed
4. Substance abuse or uncontrollable seizures
5. Bulbar-innervated muscle impairment with inability to close the glottis
6. Conditions that interfere with the use of IPPV interfaces

   (Ex. facial fractures, inadequate bite for mouthpiece entry)
7. Inadequate caregiver support

Support of daytime ventilation

- NMD progress to constant hypoventilation & requires 24hrs ventilatory support

- Recommended indications:
  1) Self extension of nocturnal ventilation into waking hours
  2) Abnormal deglutition due to dyspnea, relieved by ventilatory assistance
  3) Inability to speak a full sentence without breathlessness, and/or
  4) Symptoms of hypoventilation with baseline SpO_2 <95% and/or blood or $EtCO_2$>45 mm Hg while awake

- Patients receiving NIV should have regular (at least annual) noninvasive monitoring of gas exchange, including SpO_2 and $EtCO_2$ levels

Respiratory muscle training

- Inspiratory resistive exercise

- No definite effect on spirometry or MIP/MEP
- Respiratory muscle endurance ↑

- Conflicting results on the effect of RMT in NMD
- Not effective with patients /c FVC<25%$_{pre}$ and/or $PaCO_2$>45mmHg

- <u>Not</u> applicable in the most compromised patients

Glossopharyngeal Breathing (GPB)

- Both inspiratory, expiratory (indirectly) assist
- Patients with weak inspiratory muscles and no VC,
  When not using a ventilator or in event of sudden ventilator failure
- "gulp"
  6~9 gulps of 40~200 ml each, exceed 3000mL
  60% of ventilator users with good bulbar function
  → can use GPB & discontinue ventilator use for minutes up to all day
- Not suitable for patients with severe oropharyngeal m. weakness

Additional Management

- Pneumococcal vaccination for patients aged 2 yrs ↑
- Annual immunization /c trivalent inactivated influenza vaccine for patients 6 months ↑

- Evaluation of swallowing function

- Appropriate nutritional support (via oral or feeding tubes)
  ; nutritional problems influence the patient's pulmonary status

Additional Management

- Effect of corticosteroids on pulmonary function

Table 3 Pulmonary outcome in Class II study comparing prednisone and placebo (Mendell,[9] 1989)

Treatment	FVC, L	*p* Value FVC	MEP, mm Hg	*p* Value MEP
Placebo	1.52		14.74	
Prednisone 0.75 mg/kg/d	1.68	0.0004	17.32	0.01
Prednisone 1.5 mg/kg/d	1.66	0.002	18.19	0.001

Table 4 Pulmonary outcome in Class II study comparing prednisone and placebo (Griggs,[11] 1991)

Treatment	FVC, L	*p* Value FVC	MEP, mm Hg	*p* Value MEP
Placebo	1.48		14.64	
Prednisone 0.3 mg/kg/d	1.67	0.006	15.00	0.75
Prednisone 0.75 mg/kg/d	1.64	0.001	16.76	0.055

Neurology® 2016;86:465-472

Additional Management

- Effect of corticosteroids on pulmonary function
  - Several class III studies using deflazacort or prednisolone showed benefit in various measures of pulmonary function

- In children with DMD, *prednisone* offered for improving strength (Level B) and pulmonary function (Level B)

- *Deflazacort* maybe offered for improving pulmonary function, reducing the need for scoliosis surgery, delaying cardiomyopathy onset, and increasing survival at 5–15 years of follow-up (Level C for each)

Thank you for your attention !