Special Considerations in the Respiratory Management of Spinal Muscular Atrophy

Nonpharmacologic Airway Clearance Therapies

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“I was floating in a tunnel toward a very bright light and then a voice told me I had to go back and finish listening to the presentation.”
Neuromuscular Diseases

Ventilation

The Airway

Special notes
Neuromuscular Diseases

Special Considerations in the Respiratory Management of Spinal Muscular Atrophy
NEUROMUSCULAR DISEASE IS A VERY BROAD TERM THAT ENCOMPASSES MANY DISEASE AND AILMENTS THAT EITHER DIRECTLY OR INDIRECTLY IMPAIR THE FUNCTIONING OF MUSCLE.
Respiratory Muscles

- Amyotrophic Lateral Sclerosis Bulbar Palsy, Progressive, Muscular Atrophy, Spinal, Myasthenia Gravis, Neuralgia - Neuromuscular Diseases, Spinal Muscular Atrophies of Childhood, more........

SMA best example
The spinal muscular atrophies (SMA’s) are inherited as autosomal-recessive disorders of anterior horn cells with the genetic defect at chromosome 5q13.

Gene deletions are detectable in 98% of patients. The incidence is about 1/5000. Spinal Muscular Atrophy refers to atrophy of muscles due to loss of motor neurons within the spinal cord.
Spinal Muscular Atrophy

- Most common genetic cause of infantile death

- 2\textsuperscript{nd} most common autosomal recessive disorder:
  - \(\sim 1:6,000\) and a carrier frequency of \(\sim 1:40\)
  - Cystic fibrosis: \(1/\sim 2,000\); ALS: \(1/\sim 40,000\)
  - SMA affects all racial/ethnic groups similarly
  - 50,000 SMA cases in US/EU/Japan; 1,000 new US cases annually

- SMA results in the specific loss of motor neurons
**Spinal Muscular Atrophy (SMA)**

- Broad clinical spectrum based on age and severity

"Classic" definitions of disease - which are changing dramatically):
  - Type I (severe): death by 2 years
  - Type II (intermediate): death by 6 years
  - Type III (adult): normal life expectancy; wheelchair bound
Spinal Muscular Atrophy (SMA)

- All forms of SMA are caused by loss of a single gene: survival motor neuron (SMN1)

- SMN2: a nearly identical copy gene is a critical disease modifier and target for therapeutic intervention

**Two SMN genes: the critical difference is alternative splicing of exon 7**

- SMN2: Low full-length levels
  - Alternatively spliced product ~85% Δ7 (lacks exon 7)
  - No protection from SMA
  - Coding sequence identical to SMN1
  - Only present in humans

- SMN1: ~100% full-length SMN
  - Protects from SMA

- 500 Kb
  - SMN1
  - SMN2
  - NAIP
  - C212
  - AG1
  - T
  - C
  - A
  - C
  - C
  - T
  - T
  - 8 7 6 5 4 3 2a 2b 1 1 2a 2b 3 4 5 6 7 8

- FL SMN
- Δ7 SMN
SMA is well-suited for therapeutic intervention:
1) Single gene responsible
2) Patient population is extremely homogenous
3) SMN2 can make “good” SMN protein

These advantages are why NIH/NINDS has selected SMA as the “model” disease for a novel platform for NIH funding and drug discovery:

The SMA Project
Dr. Jill Heemskerk, NINDS
Indoprofen analogues are currently pushing towards IND (Investigational New Drug) application
The SMA Treatment Acceleration Act has been submitted to committees in the House and in the Senate.

So far we have 31 cosponsors signed on in the House and 11 cosponsors in the Senate.

We are actively pursuing additional support through lobbying on the Hill.
SPINRAZA is the first and only FDA-approved treatment for spinal muscular atrophy (SMA). In laboratory tests and animal studies, it was shown to increase full-length survival motor neuron (SMN) protein by targeting the process through which it is produced by the *survival motor neuron 2 (SMN2)* gene.
PULMONARY FOCUS

- All neuromuscular diseases produce essentially the same complications.
- Patients suffer from the same general complication in their pulmonary function tests (PFT).
  - The PFT usually shows a reduction in both the vital capacity (VC) and total lung capacity (TLC) with an increased residual capacity (RC).
Reduced respiratory muscles function
- Results in the reduced ability to generate intrathoracic pressures.

Airway obstruction
- Often the most common problem for neuromuscular impaired patients.

Ventilatory insufficiency or complete ventilatory failure

Additional complications often result from an impaired cough
- Often respiratory infections.
When ventilatory failure is imminent, ventilatory assistance is required.

Intubation followed by a tracheotomy is the common invasive ventilation choice.

The other option is non-invasive ventilation.
**Figure 2.** Correlation between prevalence rate of intensive care unit (ICU)-acquired infection and mortality rate

STAUFFER STUDY

Prospective study of the complications and consequences of endotracheal intubation and tracheotomy

n= 150

Adverse consequences

- **66 %** of all tracheotomies during placement and use of the artificial airways.
  - Stomal infection **36 %**
  - Stomal hemorrhage **36 %**
  - Excessive cuff pressure requirements **23 %**
  - Subcutaneous emphysema or pneumomediastinum **13 %**
Cuff pressures and Volumes
PREDICTORS FOR SUCCESSFUL EXTUBATION IN CHILDREN AND INFANTS

Predict
Foretell on the basis of observation, experience, or scientific reason.

Successful
Having succeeded or being marked by a favorable outcome

Common (conservative)

Successful extubation = Not requiring re-intubation after 48 hours
Re-intubation

Adults

Rates can be as high 19%

Premature Neonates

Between 22% to 28%
• “integrated indices useful in adults do not reliably predict extubation success or failure in infants and children”. 
**ADULT INDICATORS : NOT SIGNIFICANT**

- **RR** = increase or decrease showed no significant prediction of extubation failure
- **Breathing patterns** = paradoxical
  - yes 37% failure rate
  - no 16% failure rate
- **NIF** = > - 20 good predictor in adult failure showed no trend in failure and no trend with higher negative return pressures
- **RSBI** = No significant prediction
Successful extubation of mechanically ventilated patients depends:

- the capacity of the respiratory muscles to sustain spontaneous breathing
- the load placed on the respiratory muscles
- the inspiratory drive.
Extubation failures had higher RSBIs and lower CROP index values.

Children failing extubation demonstrate abnormalities of respiratory function.

RSBI and CROP index = useful in predicting the success pediatric extubation
CROP

Compliance, Resistance, Oxygenation, Pressure Index (CROP Index) (Dynamic Compliance \times Maximal Negative Inspiratory Pressure \times (Pao_2/Pao_2)/Respiratory Rate)

found that spontaneous respiratory rate \leq 45/min, spontaneous tidal volume \geq 5.5 \text{ mL/kg}, RSBI \leq 8 \text{ breaths/min/mL/kg body weight}, and Compliance, Resistance, Oxygenation, Pressure Index (CROP Index) \geq 0.15 \text{ mL/kg body weight/breaths/min} were good predictors of successful extubation
INDICATORS; SIGNIFICANT VS. FAILURE

Extubation failure increased significantly;

- Pre-extubation FIO₂ increased (30%)
- Mean airway pressure
  - <5 cm H₂ O, the failure rate was <10%, and increased significantly as mean airway pressure increased
- Oxygenation index pressure (FIO₂, MAP and PaO₂)
  - (better than FIO₂ or mean airway pressure alone)
    - The equation is:
      \[ \text{OI} = \frac{\text{F} \text{iO}_2 \times \text{MAP}}{\text{PaO}_2} \]
    - Significance: 2 = Superman    33 = ECMO
INDICATORS; SIGNIFICANT VS. FAILURE

Total minute ventilation provided by the ventilator

- Extubation failure was low when total minute ventilation provided by the ventilator was ≤ 20%
- Extubation failure increased significantly when total minute ventilation provided by the ventilator increased

Increased load on the respiratory muscles

- Low dynamic compliance
  - Higher success rate (>.9)
  - Lower success rate (<.4)
- Decreased inspiratory drive
  - Decreased mean inspiratory flow
WHOA! ALL OF THIS NEW COMPUTER SURGICAL EQUIPMENT IS COMPLICATED!
WHERE DID YOU TRAIN... HARVARD? COLUMBIA?

PLAYSTATION
NEUROMUSCULAR
Ventilator weaning is attempted without permitting hypercapnia.

- Afebrile
- No supplemental oxygen requirement to maintain SpO2 >94%
- Chest radiograph abnormalities cleared or clearing
- All respiratory depressants discontinued
- Airway suctioning required less than 1-2x/eight hours
- Coryza diminished sufficiently so that suctioning of the nasal orifices is required less than once every 6 hours.
  - This is important to facilitate use of nasal prongs/mask for post-extubation nasal ventilation.
- Extubation to continuous nasal BiPAP ventilation and little or no supplemental oxygen.
Because of compensation no one indicator will predict failure.

Rather a composite picture must be evaluated for sufficient physiological function to support unassisted ventilation
Ventilation
Hypercapnea generally begins to occur when the respiratory muscles are below 50% efficiency and is proportional to the severity of muscle function.

Microatelectasis can become a major threat to this population and may not show in initial radiological exams.
With CO2 retention or ventilator synchronization, difficulties may be eliminated by improved nasal interface, increase in pressure support and ventilator rates or a change from BiPAP to using a volume-cycled ventilator.

Persistent desaturation despite eucapnia and aggressive use of expiratory aids indicate impending respiratory distress and need to re-intubate.
This is an option for the more functional and independent patient. This is not for everyone but the patients that use this system will not part with it. They do require a nasal set up for nocturnal support.
New ventilators for both acute care and home use have incorporated NIV features.
Nonpharmacologic Airway Clearance Therapies
Airway maintenance is one of the most important components of the management of neuromuscular-impaired patients. It significantly increases the success of extubation and the outcomes in non-invasively ventilated patients.

4 (J. Bach et al., 2002; JR. Bach et al., 2000; JR. Bach et al., 1998)
A mini-symposium on mucus:

“The Primary goal of airway clearance is to facilitate bronchial mucus transport and sputum expectoration”

Radioactive tracers were used to determine the effectiveness of clearance.

Results showed that PFT’s were not a reliable method of evaluation and that subjective patent evaluation was a better technique.
**JUST CAN’T DO IT ALONE**

- Patients with airway obstructions or impairment require intervention to assist in the elimination of mucus from the airway.
- Airways cleared of mucus improve ventilation and reduce the negative effects of the obstructed airway.
The normal process for clearing secretions in a healthy person without need of any assistance is the model that is used in the therapy for airway clearance.

- LOOSENING THE SECRETIONS
- MOBILIZING THE SECRETIONS
- COUGHING UP THE SECRETION
- EXPECTORATING THEM

Airway clearance therapy is evidenced-based techniques that duplicates these actions allowing a caregiver to assist in maintaining a clear airway.
HOW DO WE DO IT

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Chest physical therapy (CPT) is the second step in the complete airway management of this type of patient. CPT is performed to help dislodge secretions, for removal, that are normally loosened during ambulation.

If there are no secretions to be dislodged then CPT will not be required.

CPT consists of two parts, percussion and vibration, that can be applied together or individually.
CF STYLE

Left lung

front

lateral views

back

medial views
PICK YOUR WEAPON
☐ INCOURAGE QUICK START PROTOCOL
TREATMENTS/DAY: 2, MINUTES/TREATMENT: 30, FREQUENCIES: 6-15 HERTZ, MINIMUM USAGE/DAY: 10 MINUTES
PRESSURE: 60-100% (OR AS TOLERATED BY PATIENT).

☐ AFFLOVEST SUGGESTED PROTOCOL
TREATMENTS/DAY: 2, MINUTES/TREATMENT: 30, MINIMUM USE/DAY – 10 MINUTES, FREQUENCIES – 5 TO 20 HERTZ (OR ADJUSTED PER PATIENT COMFORT AND THERAPEUTIC BENEFIT).

Unit nearly 30% quieter
HOW DO WE DO IT

The normal process for clearing secretions in a healthy person without need of any assistance is the model that is used in the therapy for airway clearance.

- **LOOSENING THE SECRETIONS**
- **MOBILIZING THE SECRETIONS**
- **COUGHING UP THE SECRETION**
- **EXPECTORATING THEM**

Airway clearance therapy is evidenced-based techniques that duplicates these actions allowing a caregiver to assist in maintaining a clear airway.
MOBILIZING THE SECRETIONS

Postural drainage

- Postural Drainage Therapy defines Postural drainage as “therapy designed to improve the mobilization of bronchial secretions and the matching of ventilation and perfusion, and to normalize functional residual capacity (FRC) based on the effects of gravity and external manipulation of the thorax”\(^9,10\).
THIS THERAPY NEED NOT BE DONE WITH A COMPLETE CLINICAL FEEL TO IT.
HOW DO WE DO IT

The normal process for clearing secretions in a healthy person without need of any assistance is the model that is used in the therapy for airway clearance.

- Loosening the secretions
- Mobilizing the secretions
- Coughing up the secretion
- Expectorating them

Airway clearance therapy is evidenced-based techniques that duplicates these actions allowing a caregiver to assist in maintaining a clear airway.
Coughing Up the Secretion

Cough

- The successful elimination of mucus will depend on the degree of effectiveness of a natural cough.

A cough has three phases
1. The inspiratory component that leads to a
2. Compression phase then
1. The explosive exhalation with flows that causes an energy transfer to the mucus that transports it out of the airway.¹²
A good cough is one of the most important airway clearance tools to the neuromuscular impaired patient but often for this type of patient it is least effective.
FORCED EXPIRATORY TECHNIQUE (FET)

- The AARC guidelines describe the FET as “huff coughing”

- This is generally about two forced exhalations (huff’s) with the glottis open and then a rest period.
The thrust is a type of Heimlich maneuver that uses the diaphragm to help compress the air in the lungs augment the expiratory flow.\textsuperscript{15}

pushing on the upper abdomen in synchrony with the patient’s own cough effort.
Mechanical assistance; produces positive and negative pressures.

Peak flow's can be significantly increased and can simulate a cough flow.
BRONCHOSCOPE DURING ACTIVE IN-EXSUFFLATION (COUGHOLATOR / COUGH ASSIST) AT PRESSURES OF +40 / -40
Flow rate is the volume of fluid per unit time flowing past a point through the area $A$. Here the shaded cylinder of fluid flows past point $P$ in a uniform pipe in time $t$. The volume of the cylinder is $Ad$ and the average velocity is $\bar{v} = \frac{d}{t}$ so that the flow rate is $Q = \frac{Ad}{t} = A\bar{v}$.

$Q = V \times A$

Pressure = Flow x Resistance

$P = \frac{\text{Force}}{A}$
When a tube narrows, the same volume occupies a greater length. For the same volume to pass points 1 and 2 in a given time, the speed must be greater at point 2. The process is exactly reversible. If the fluid/gas flows in the opposite direction, its speed will decrease when the tube widens.
The optimal pressures set for mechanical assistance is at about +40 cm H2O to -40 cm H2O pressures.

In one study using a standard lung model for 10 full cycles, flow pressures were measured. The findings showed the pressures of +/- 40 cmH2O to be the best setting to generate exhalation flows of greater than 2.71 l/sec.

A normal cough has flow ranges of 6 to 20 l/sec.
Maximal insufflations are extremely important to increase peak cough flow (PCF) for patients with neuromuscular conditions who have VCs of < 1500 ml.

There have been studies performed with pressures lower than 40/-40 cmH2O but the methods were questionable and the results were poor.
BRONCHOSCOPE DURING ACTIVE IN-EXSUFFLATION (COUGHOLATOR / COUGH ASSIST) AT PRESSURES OF +40 / -40
For timing a cadence of “1-2-3” (inspiratory) spoken out loud followed by the word “COUGH” and finally followed by “1-2-3” (expiratory).

• This is an important part of the process because the patient, CoughAssist TM and therapist or caregiver must work in unison.

Each session of airway clearance consists of several sets of multiple cycles of insufflation-exsufflation.
Each session of airway clearance consists of several sets of multiple cycles of insufflation-exsufflation.

- Sets of 3, for basic maintenance, may be increased to 5 for aggressive secretion expulsion.

- Three cycles, per set, are consecutively applied without removing the mask for suctioning for routine maintenance, and increased to 5 when you need to be more aggressive.

- Insufflation and exsufflation are usually at the same pressure and duration. (ATS consensus) Abdominal thrusts are applied during the exsufflation phase of each cycle.
HOW DO WE DO IT

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- EXPECTORATING THEM

Airway clearance therapy is evidenced-based techniques that duplicates these actions allowing a caregiver to assist in maintaining a clear airway.
Suctioning;
the upper airway (oropharynx)
lower airway (trachea bronchi).
A rigid Catheter, Yankauer, can be used for the mouth and
the back of the mouth. For deeper suctioning a flexible
catheter is required.

The AARC (American Association for Respiratory Care) guidelines are generally followed

The AARC has specific guidelines for suctioning of the patient in the home
SOFT NASAL SUCTION
Special Notes
Scheduled routine treatments should be avoided

The patient’s specific clearance needs determine the treatment times and intensity.

Generally, the morning requires a very aggressive treatment and the evening requires a moderate treatment for sleep.

As with all therapies for airway clearance of neuromuscular patients, if secretions increase, then the therapy must be increased. A nonproductive session may be experienced regardless of quality of the effort.

If the vital signs are good and the patient is stable, it is best to leave the patient for a short time (maybe ½ hour) and then reattempt. This is common and most likely to occur in the morning.

Respiratory therapists, nurses, and all healthcare workers should begin the training of the family immediately. They can begin to synchronize with the patient's needs so that when they provide care at home they will be competent and comfortable.
Rest is essential to the recovery of a patient. This is a basic universal concept required to strengthen the patient to be able to give the best effort and be able to physically and mentally tolerate the therapy
There is a problem with the introduction of O2.

Oxygen, while essential for recovery of the patient from distress or failure, increases the risk of complications when delivered to a neuromuscular impaired patient.

The typical routine indiscriminate use of supplemental O2 negates the value of oximetry in gauging alveolar ventilation and airway secretion management.
There is a situation when it is very important to use oxygen during therapy. When normal suctioning, the practitioner should pre- and post-oxygenate the patient.

During therapy, if saturation falls below acceptable limits, oxygen can be used via bag mask ventilation to recover.
TREATMENT GOALS

Optimize chest wall/lung ROM and growth
Optimize cough flows
Maintain normal ventilation
OUTCOMES

Example SMA type 1

- difference in invasive and non-invasive ventilation outcomes, was not statistically significant. 26
- hospitalizations decrease after 5 years when ventilated non-invasively and infections increase after 5 years with tracheotomies. 25
- There are additional benefits -the freedom from daytime ventilation and the ability to speak. 27
- In younger groups of children, the use of non-invasive home based ventilation is common but still likely to require further PICU admission. 28
"There is no reason for any individual to have a computer in their home." --- Kenneth Olsen, 1977 President and founder of Digital Equipment Corp.
"Airplanes are interesting toys but of no military value." --- 1911, J. Marshal Ferdinand Foch, French Military Strategist and future World War I commander
"Man will never reach the moon regardless of all future scientific advances." --- February 25, 1967, Dr. Lee de Forest, inventor of the Audio Tube (Television), and Father of Radio.
"[Television] won't be able to hold on to any market it captures after the first six months. People will soon get tired of staring at a plywood box every night." --- 1946, Darryl F. Zanuck, head of 20th Century-Fox.
"We don't like their sound. Groups of guitars are on the way out.”---1962, Decca Records rejecting the Beatles.
"For the majority of people, the use of tobacco has a beneficial effect." --- November 18, 1969, Dr. Ian G. MacDonald, Los Angeles surgeon, as quoted in Newsweek.
"This 'telephone' has too many shortcomings to be seriously considered as a means of communication. The device is inherently of no value to us." --- 1876, Western Union Internal memo.
"Nothing of importance happened today." --- July 4, 1776, written by King George III of England
“Everything that can be invented has been invented." --- 1899, Charles H. Duell, U.S. Commissioner of patents.
Airway Maintenance of the Non-Invasively Ventilated Neuromuscular Impaired Patient

Welcome to the virtual clinical pathway for airway clearance. Although this pathway can be applied to any patient, the focus is on non-invasively ventilated neuromuscular-impaired patients, mainly because this type of patient requires a good deal of airway maintenance. Because this is such a significant part of the care for the neuromuscular-impaired patient, I created this virtual clinical pathway to establish a consistent, effective and evidenced-based method of maintaining the airway.
I will apply, for the benefit of the sick, all measures [that] are required, avoiding those twin traps of overtreatment and therapeutic nihilism.

Nihilism; a belief that life is pointless and human values are worthless
QUALITY OF LIFE; LOOKS LIKE THEIR STUCK TO BED AND THE VENT


Informatics, Nursing 21(5): 259-264.


*WordNet® 3.0, © 2006 by Princeton University*

The Washington University School of Medicine, Neuroscience Tutorial.

[http://thalamus.wustl.edu/course/spinal.html](http://thalamus.wustl.edu/course/spinal.html)


ATS Consensus, 2004

JR Bach, 2002
Hadjikoutish, Wiles, & Eccles, 1999; Sivasothy, Brown, Smith, & Shneerson, 2001
Sivasothy et al., 2001.
Sancho, Servera, Diaz, & Marin, 2004) (Hanayama et al., 1997) (Winck et al., 2004
(Kang & Bach, 2000)
(Gomez-Merino & Bach, 2002; Gómez-Merino et al., 2002; Sancho et al., 2004
Hanayama et al., 1997; Winck et al., 2004)


That's all Folks!