



MYOTONIC  
DYSTROPHY  
FOUNDATION

Care and a Cure



2018  
MDF ANNUAL CONFERENCE  
September 14-15, 2018  
Nashville, TN

# BREATH EASY: PULMONARY SYMPTOM MANAGEMENT

Valeria A Sansone, MD PhD



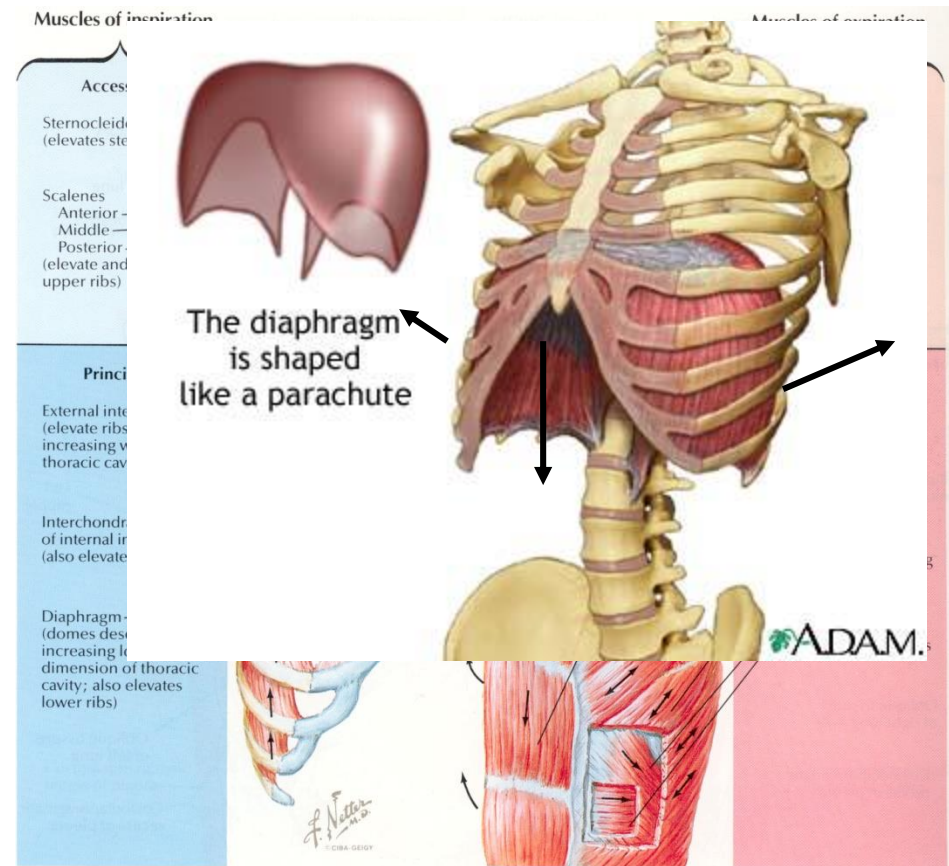
# Overview

- **The Respiratory System**
  - The lungs and the respiratory muscles: what do they do
  - Breathing and sleeping: what happens at night
- **What goes wrong in Myotonic Dystrophies**
  - Respiratory muscle weakness
  - Weak cough
  - Sleep-related breathing problems
- **Why should we care about the respiratory system?**
- **What can we do?**
- **The Respiratory Care Recommendations for Adults with Myotonic Dystrophies**
  - What to look for
  - How? Which tests?
  - Management: what to do

# THE RESPIRATORY SYSTEM

# Respiratory Muscles

- **Inspiratory:** muscles increase thoracic volume, intrapleural and alveolar pressures fall. Air is drawn in to lungs.
  - Diaphragm
  - External intercostals
  - Scalene, sternocleidomastoid
- **Expiratory:** Largely passive
  - Abdominal muscles
  - Internal intercostals



# The Lung's Main Function

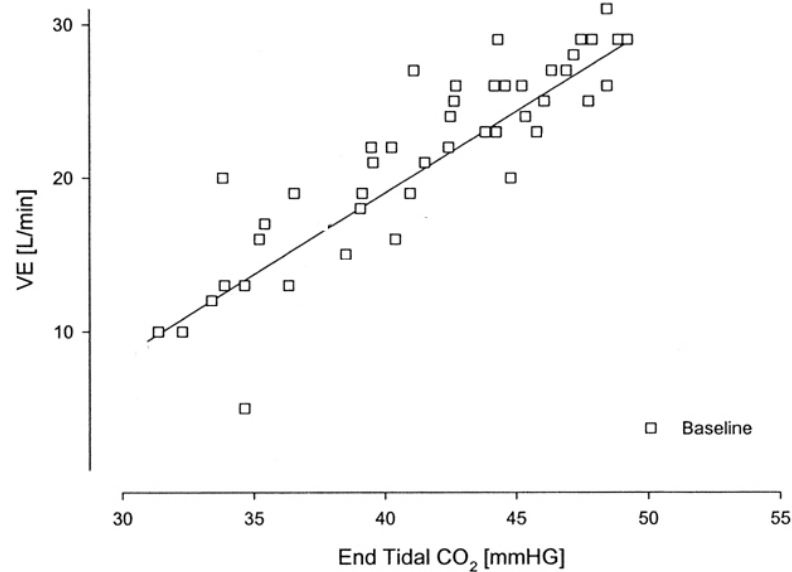
---

- Get Oxygen into the body & blood stream
  - ▣ Blood carrying oxygen goes to the heart
  - ▣ Heart pumps it to all the organs
- Get rid of carbon dioxide
  - ▣ Our bodies produce carbon dioxide (CO<sub>2</sub>)
  - ▣ When we exhale, we blow out carbon dioxide

# Control of Ventilation (Breathing)

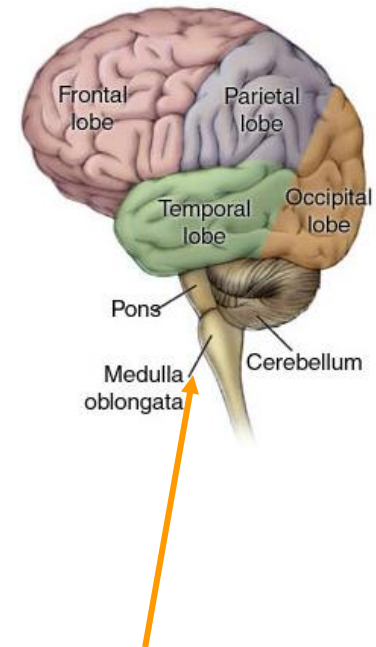
- Major Mechanism:

- Sensors in the brainstem respond to carbon dioxide levels



- Minor mechanism:

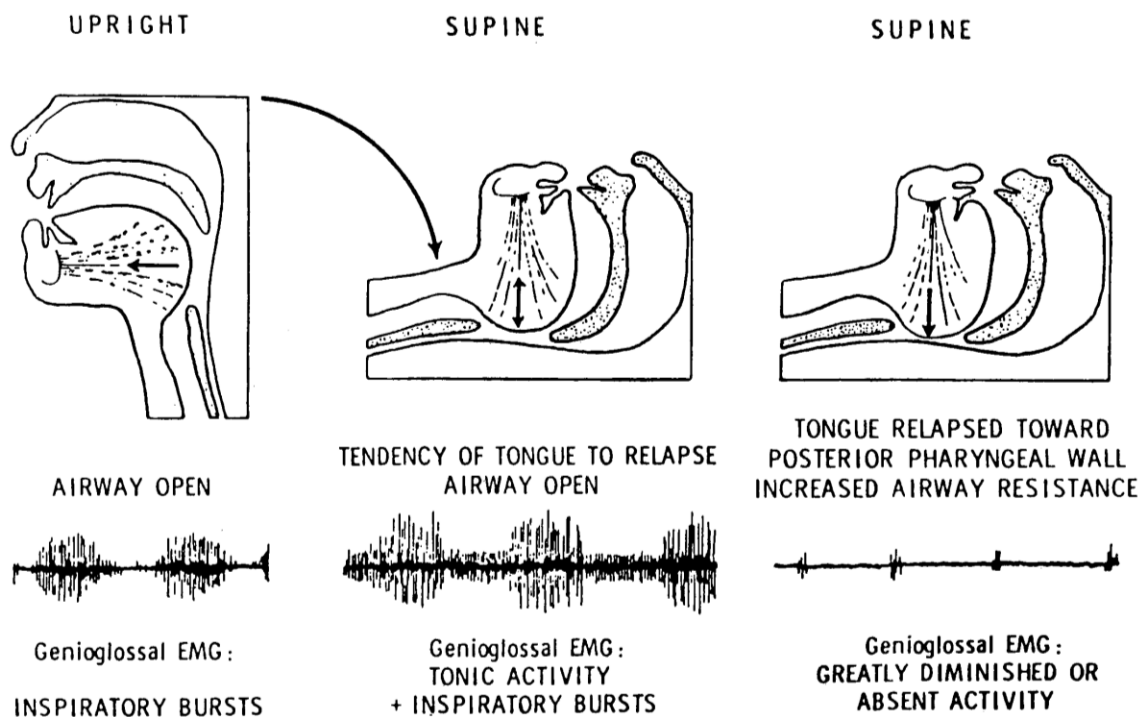
- sensors respond to low oxygen levels



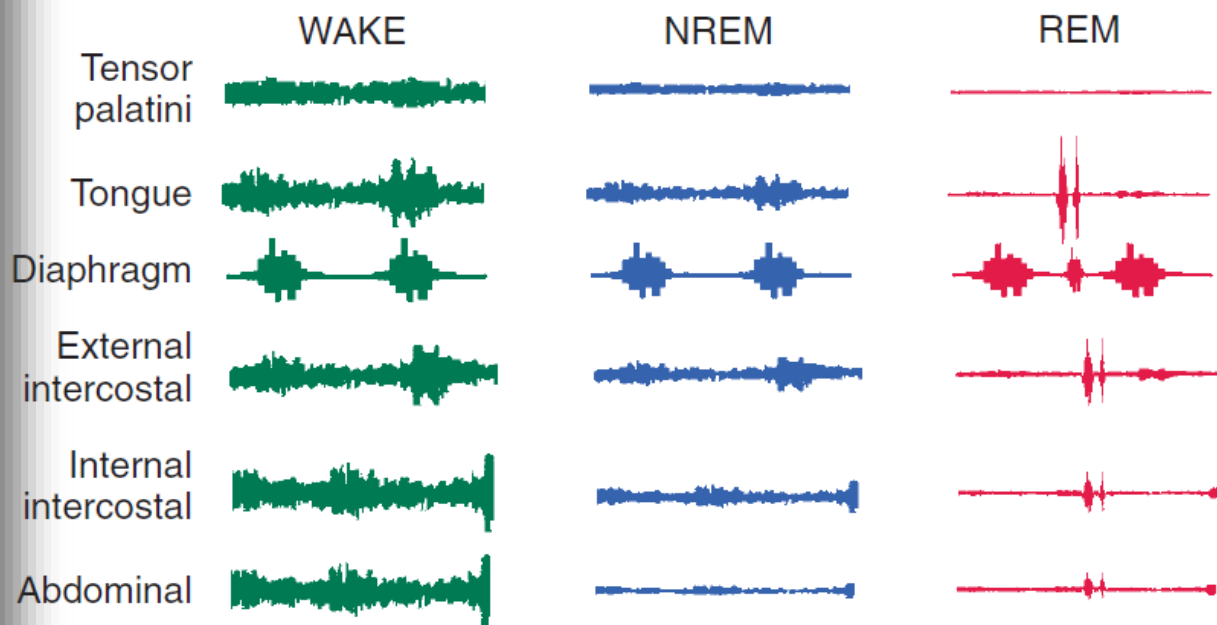
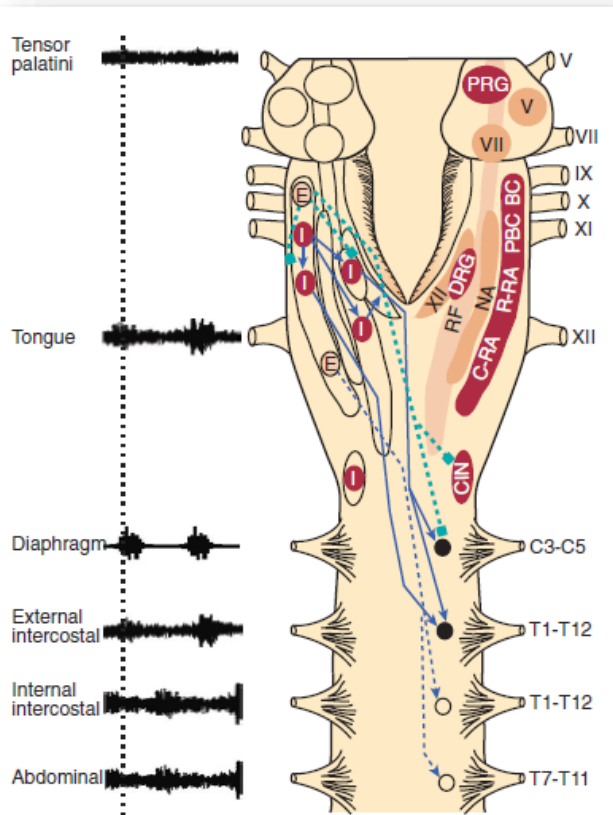
# What happens at night? Breathing and Sleeping

When we switch from daytime to night/sleep

- the activity of most respiratory muscles is reduced
- air encounters more resistance in the upper airways when supine
- the ability of respiratory muscles to adapt to  $\text{CO}_2$  and  $\text{O}_2$  variations is reduced

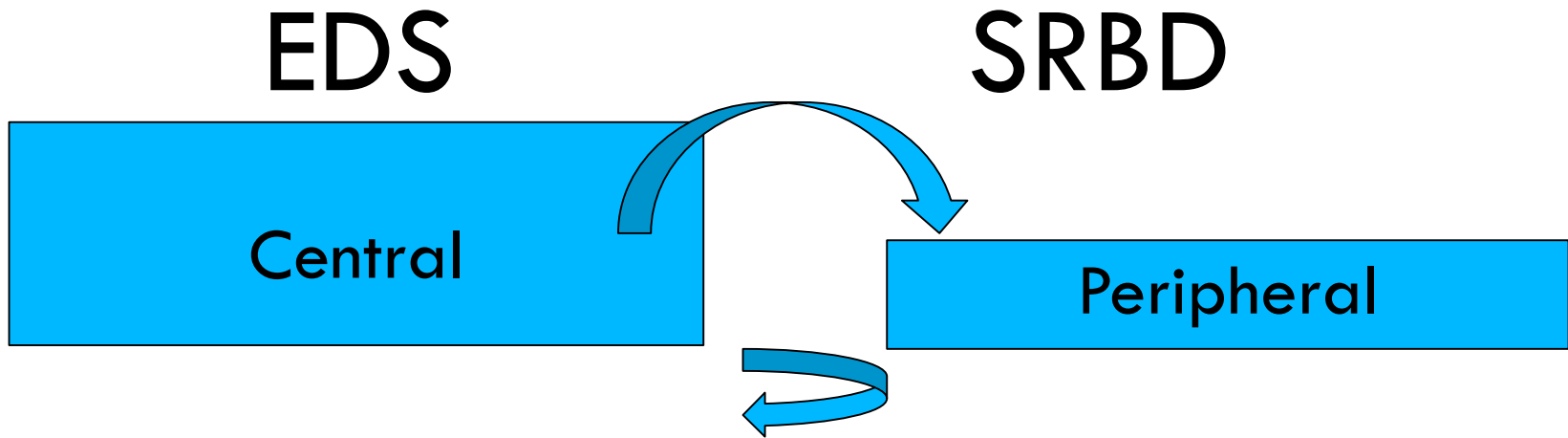


# What happens at night? Breathing and Sleeping

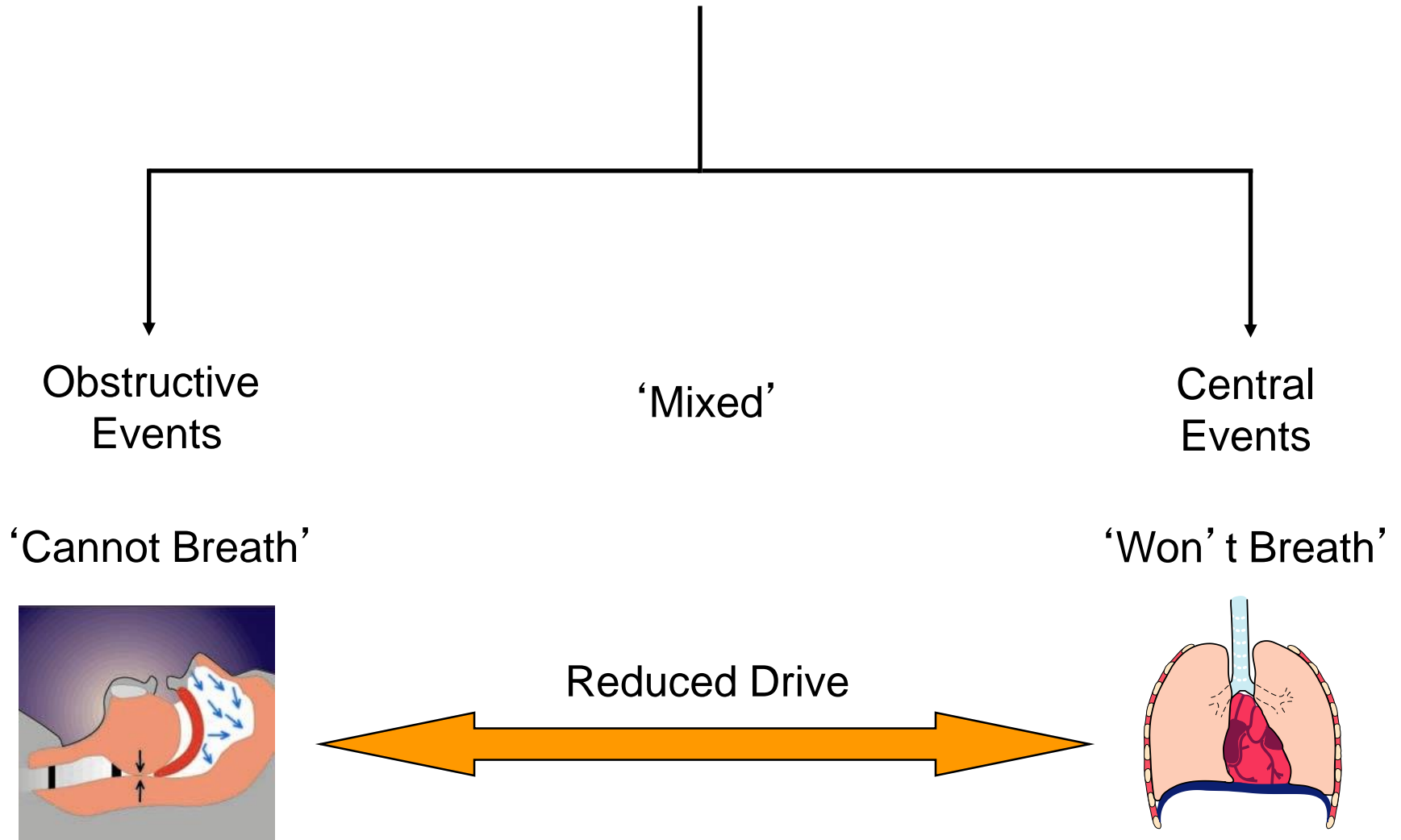




# Sleep and Breathing Disorders






# Terminology of Sleep Apnea



# WHAT GOES WRONG IN DM

# What goes wrong in DM

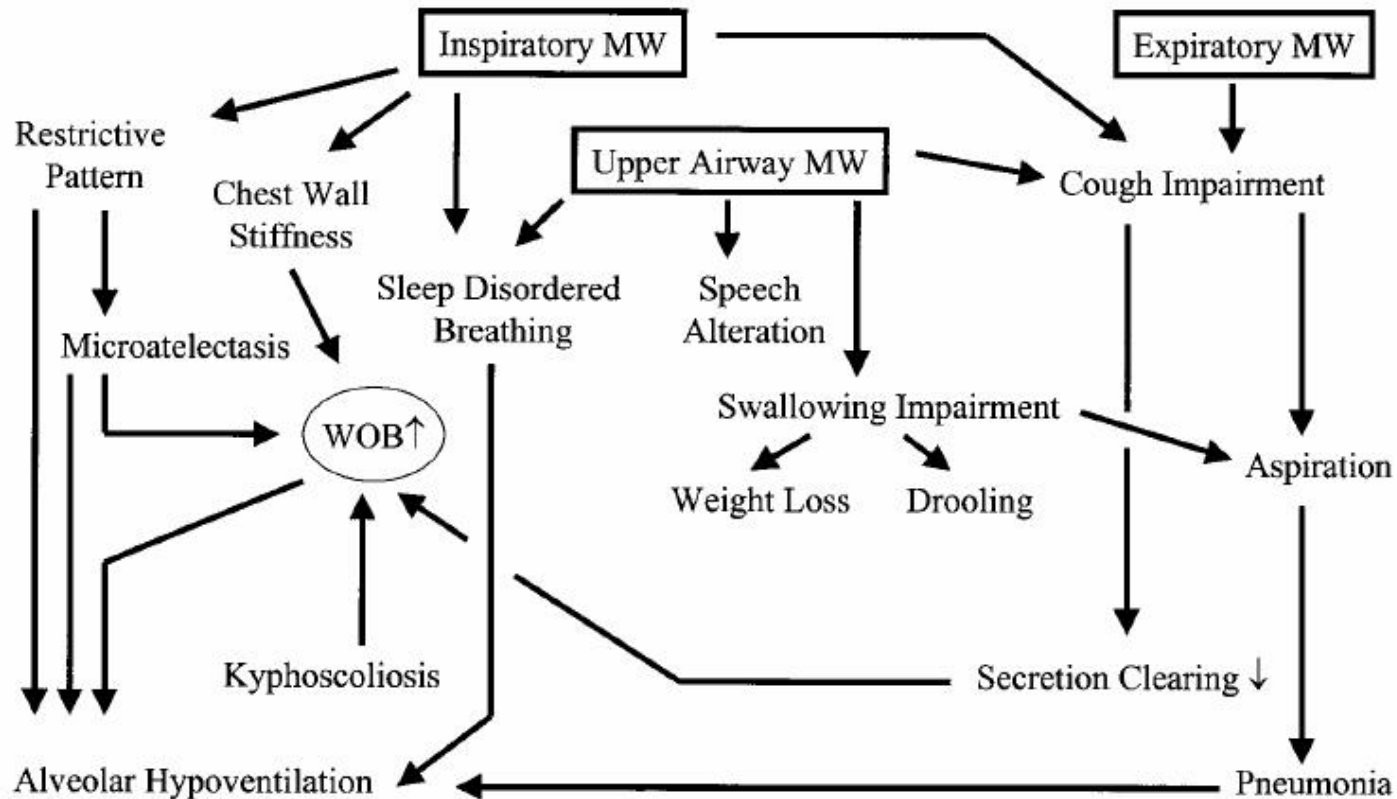
## 3 main issues

1. Weak muscles  problems with gas exchange (mainly during the day)
2. Reduced cough  problems with secretions (mainly during infections/peri-surgery)
3. «lazy» centers in the CNS for breathing/sleep  sleep-related breathing disorders

WHY SHOULD WE CARE?

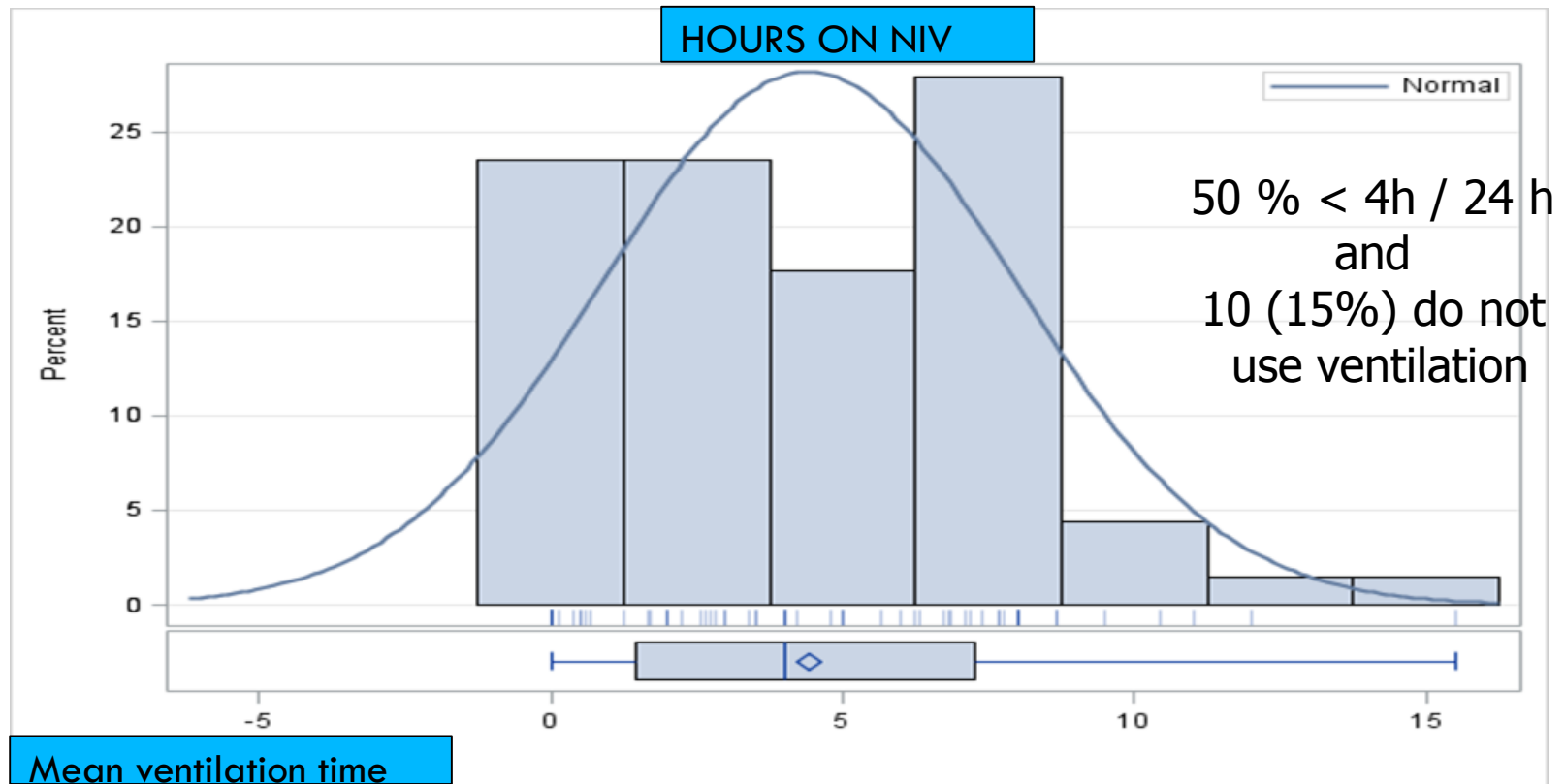
# Why should we care

Respiratory complications are a major cause of **morbidity** and **mortality** in neuromuscular disorders in general, and in DM



# Why Should We Care?

SCD death occurs more frequently in patients who should be on NIV and who are not using it



What can we do?



# What can we do?

*but....*

- ANY CURE WILL BE AN **ADD-ON** IN THE PATHWAY OF CARE
- IT WILL **NOT REPLACE** RECOMMENDATIONS FOR STANDARDS OF CARE

# What can we really do?

## **IN GENERAL:**

- Help more patients receive better respiratory care
- Promote knowledge and diffusion/implementation of respiratory SoC amongst non-DM specialists
- Identify patients who are at risk for respiratory problems
- Promote treatment of respiratory symptoms or problems
- Facilitate research by harmonizing patient care and create the best milieu any drug can work in

# What can we really do?

---

1.GET YOUR REGULAR VACCINATIONS

2.MAKE SURE YOU GET REGULAR  
PULMONARY CONSULTATION

3.CHECK YOUR WEIGHT!!

4.MIND YOUR SWALLOWING

# What can we really do?

## Orthopnea

- |    |  |  |
|----|--|--|
| a) | Do you feel short of breath when you lie down?                                 |  |
| b) | Do you need to sleep with more than 1 pillow because you feel short of breath? |  |
| c) | Do you sleep sitting in a chair or arm-chair because you feel short of breath? |  |

## Dyspnea when performing activities of daily living

- |    |   |  |
|----|---|--|
| a) | Do you feel short of breath when you move around the house? |  |
| b) | Do you feel short of breath when you wash or dress?         |  |
| c) | Do you feel short of breath when you talk?                  |  |

# What can we really do?

---

**#3**

**DO AIR-STACKING EXERCISES TO  
INCREASE LUNG VOLUME**

# AIR-STACKING

- Air-stacking = bringing in more air into your lungs with different techniques until max lung volume is obtained
- Insufflation techniques should be considered when FVC is  $\leq 2L$  or is  $\leq 50\%$  predicted or if there is evidence of weak cough.
- Can be done using
  - AMBU bag
  - ventilator
  - thoraco-abdominal thrust
  - cough-assisted devices P  
(if PCEF  $< 270$  L/min)
- To be used if VC  $< 70\%$  predicted
- Need to check for glottic competence
- Using an abdominal band can facilitate thoracic expansion
- Needs to be repeated for 15 minutes, 2-3 times a day



# What can we really do?

---

**#4**

**USE THE VENTILATOR AT LEAST  
4 HOURS A DAY EVERY DAY**

# TREAT WITH: Non-invasive ventilation

According to the ENMC workshop (2014) NIV should commence when there is at least one or more daytime or nighttime symptoms suggestive of chronic insufficiency in combination with:

- Daytime hypercapnia,  $\text{PaCO}_2 \geq 45$  mmHg (6.0 kPa) or
- $\text{FVC} < 50\%$  of predicted based on the best of 3 measures and  $\text{MIP} < 60$  cmH<sub>2</sub>O or
- Evidence of nocturnal hypoventilation, such as:
  - i. A rise in  $\text{PaCO}_2$  of  $\geq 8$  mmHg (1 kPa) between evening and morning ABGs or other accurate CO<sub>2</sub> surrogate;
  - ii. A rise in  $\text{TcCO}_2$  or  $\text{ETCO}_2 > 50$  mmHg (6.7 kPa) for more than 50% of total sleep time;
  - iii. While not ideal - when a measure of CO<sub>2</sub> is not available - nocturnal oximetry demonstrating sustained oxygen desaturation ( $\text{SpO}_2 \leq 88\%$  for 5 consecutive minutes or  $\text{SpO}_2 < 90\%$  for  $> 10\%$  of total sleep time.
  - iv. A lab polysomnogram showing evidence of sleep disordered breathing with  $\text{AHI} > 5$ ,  $\text{ODI} > 5$ , and  $\text{TcCO}_2/\text{ETCO}_2$  changes as above



# TREAT WITH: Non-invasive ventilation (BiPAP)

- NIV is recommended for patients who have chronic respiratory insufficiency and who have sleep-related breathing disorders.
- Delivers positive pressure
  - Inflates lungs
- Start using at night
- Can use during day as needed
  - Some use ~24hrs a day



# Which ventilator?

## At home

- With or without internal battery
- With humidifier
- Low-flow oxygen modality



# Which ventilator?







- portable



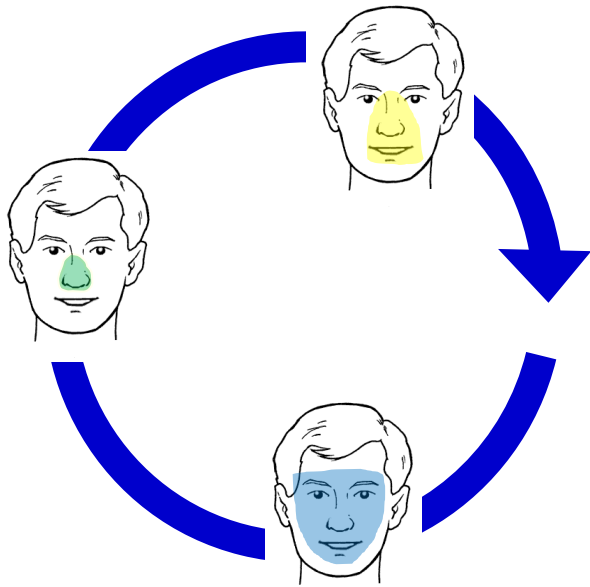
# TREAT WITH: NIV- which mask?

- Finding the correct mask is important



FACE	NASAL	NASAL PILLOWS	TOTAL	MOUTHPIECE - ORAL	HELMET
					
nose and mouth	nose	nostrils	nose, mouth, eyes	mouth	head

## Rotational strategy - change pressure points



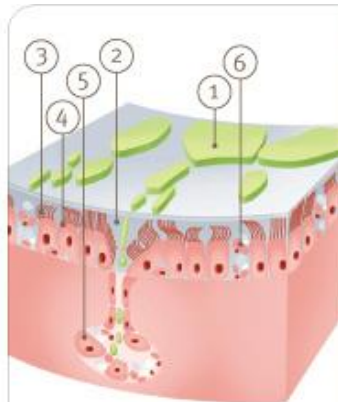
Tailoring and alternating different types of interface according to patient's needs, tolerance, and cooperation may thus be an interesting approach for reducing the side effects of noninvasive ventilation and improving its performance. This may warrant further studies.

**Brochard L**, Critical care medicine 2000

monitoring skin, marks on face

# Humidifiers

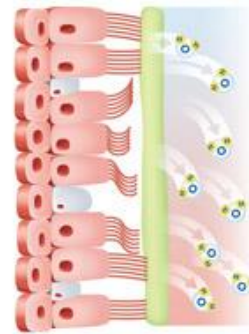
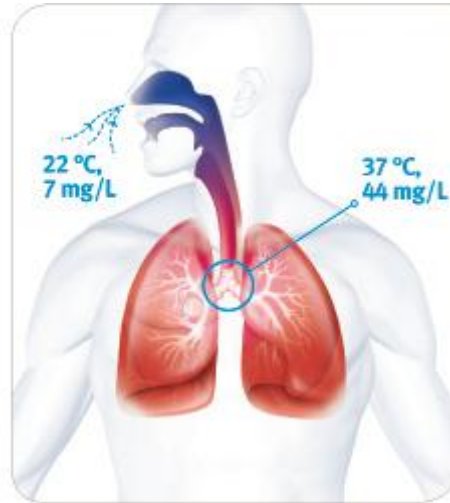
- Humidifiers with NIV may be an important option (the nose is a natural humidifier)
- The choice of having a humidifier during NIV depends on the patient's comfort and compliance



**Mucociliary Transport System**

- 1 Mucus
- 2 Aqueous layer
- 3 Cilia
- 4 Epithelium cell layer
- 5 Submucosal gland
- 6 Goblet cell

Adapted from Williams et al (1996)



# Non-Invasive Ventilation: Concerns

- Most Common Problems:
  - ▣ Skin irritation/breakdown
  - ▣ Nasal congestion or drainage
  - ▣ Claustrophobia / not comfortable with mask and BiPAP
- Common Solutions
  - ▣ Different mask / alternate masks
  - ▣ Heat & humidify air
  - ▣ Decongestants / nasal sprays
  - ▣ Gradually increase use and pressure of BiPAP



# NIV- compliance

- Compliance should be monitored
- Minimum threshold of 4 hours/day (reimbursement concerns: Medicare = 4 hrs > 75%)
- It is preferable to use NIV at night for sleep.
- Some individuals may require desensitization to the NIV during the day.
- Compliance to NIV has been reported to be lower in patients:
  - with no subjective symptoms of respiratory failure
  - High body mass index
  - in the presence of excessive leaks.

# Non-Invasive Ventilation: Benefits

- Expand lungs/prevent atelectasis
- Preserve thoracic range of motion
- Decrease shortness of breath
- Improve sleep quality
- Improve “Quality of Life”
- Improve cognitive function
- Prolong survival
  - Greater effect than any medication or other treatment

# What else can we really do?

---

**# 5**

**USE COUGH-ASSISTED DEVICES  
REGULARLY**

# Manual and mechanical cough-assisted devices

- Air-stacking = bringing in more air into your lungs with different techniques until max lung volume is obtained
- Insufflation techniques should be considered when FVC is  $\leq 2L$  or is  $\leq 50\%$  predicted or if there is evidence of weak cough.
- Can be done using
  - AMBU bag
  - ventilator
  - thoraco-abdominal thrust
  - cough-assisted devices P (if PCEF  $< 270$  L/min)
- To be used if VC  $< 70\%$  predicted
- Need to check for glottic competence
- Using an abdominal band can facilitate thoracic expansion
- Needs to be repeated for 15 minutes, 2-3 times a day



# Mechanical In-Exsufflation or Cough Assist

- Applies positive (+) pressure to the airways then rapidly shifts to a negative (-) pressure
- Can generate peak cough flow of 300-660 L/min to simulate a cough
- Delivered via mask, mouthpiece, trach tube



# Cough Assist – how?

- 2-4 sessions per day
  - 1 session = 3-5 treatments
  - 1 treatment = 3 to 5 cycles
  - 1 cycle = 1 insufflation and 1 exsufflation
- Best before meals and at bedtime
- Can also use any time secretions are present
- Avoid hyperventilation – no more than every 10 minutes

# Cough Assist Video



# TREAT WITH: airway clearance devices

- A vest can be used as a supplement to standard cough assistance techniques
- Intermittent Positive Pressure Breathing (examples of devices available) can be used by the patient alone, even with hand weakness, but requires good lip strength to correctly hold the mouthpiece.

VEST  
Percussionnaire  
...





# High Frequency Chest Wall Oscillation (HFCWO) – “The Vest”

- Vibration and chest compression loosen mucus and make it easier to cough out
- Recent study showed lower health care costs after getting a vest
- Can be used in conjunction with cough machine



# What can we really do?

---

**# 6**

**CONSIDER MODAFINIL IF  
EXCESSIVE DAYTIME SLEEPINESS**

# EXCESSIVE DAYTIME SLEEPINESS

- Excessive daytime sleepiness (EDS) is a concern for 20% of patients



- It may be the presenting symptom of DM



- It is treatable, but only a minority are on modafinil

# Excessive daytime sleepiness

Excessive  
daytime  
sleepiness

Central origin

Respiratory  
cause

mixed origin

Provigil® 200 mg Tablets

Modafinil

Take only as directed by your physician

POM

30 tablets

TEVA



+

Provigil® 200 mg Tablets

Modafinil

Take only as directed by your physician

POM

30 tablets

TEVA

# RCT using modafinil + NIV

(GUP15004\_EudraCT 2016-000601-36)



**A MULTICENTER, RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED (RCT) CLINICAL TRIAL ON THE CLINICAL EFFICACY OF NON-INVASIVE VENTILATION AND MODAFINIL ON EXCESSIVE DAYTIME SLEEPINESS IN MYOTONIC DYSTROPHY TYPE 1 (DM1)**

**PHASE I:**  
SCREENING/RECRUITMENT  
Inclusion criteria for DM1:  
> 18 yrs; CTG E1, E2, E3  
Expected n = 100

**PHASE II: NIV OPTIMIZATION**  
(defined as normal ABG and nocturnal oxymetry) > 4 hrs at least 5 days/week

**PHASE III: RANDOMIZATION**  
Pts with indication for NIV stay on NIV

**PHASE IV: INTERVENTION**

**PHASE V: COMPLIANCE + ASSESSMENT OF CLINICAL EFFICACY OVER TIME**

RESPIRATORY ASSESSMENTS + PSG + MSLT

**DM1 PATIENTS WITH EDS WITH INDICATION FOR NIV (GROUP 1)**

Expected n = 50

**DM1 PATIENTS WITH EDS WITH NO INDICATION FOR NIV (GROUP 2)**

Expected n = 30

*1 month*

RESPIRATORY ASSESSMENTS + PSG + MSLT (GROUP 1 ONLY) + ESS + FDSS + FSS + MWT + ACTIGRAPHY + MOTOR ASSESSMENTS + COGNITIVE ASSESSMENTS + QoL

**DM1 PATIENTS WITH RESIDUAL EDS/EDS (GROUPS 1 + 2)**

Expected n = 80

placebo

*3 months*

modafinil

REPEAT RESPIRATORY ASSESSMENTS + DOWNLOAD SD + ESS + FDSS + FSS + MWT + ACTIGRAPHY + MOTOR ASSESSMENTS + COGNITIVE ASSESSMENTS + QoL

placebo

*3 months*

modafinil

REPEAT RESPIRATORY ASSESSMENTS + DOWNLOAD SD + ESS + FDSS + FSS + MWT + ACTIGRAPHY + MOTOR ASSESSMENTS + COGNITIVE ASSESSMENTS + QoL

# What can we really do?

---

**# 6**

**HELP YOUR DOCTOR KNOW  
ABOUT RESPIRATORY PROBLEMS  
IN DM**

# PRIOR TO SURGERY

---

Clearance capacity and other respiratory assessments **MUST BE INVESTIGATED** prior to surgery.

If needed, adaptation to nocturnal noninvasive ventilation or to cough-assist devices should also occur prior to surgery.



# ANTIBIOTICS

---

- Be aggressive

# TO BE AVOIDED

- Mucolytics
- Oxygen on its own
- Pulmonary respiratory exercises



# WEANING AFTER TRACHEOSTOMY

After acute respiratory distress or after surgery.

- Weaning must be progressive
- Repeated free breath trials are preferred until the patient has completed 8 consecutive hours without a ventilator
- Do not use spontaneous mode with pressure support due to respiratory instability
- Consider cough assistance before and after extubating
- Relay with patients own ventilation (previously ventilated) or NIV if alveolar hypoventilation is observed
- Extubation should not be completed on surgery table
- Extubation should proceed in a recovery room or ICU due to side effects of anesthetics and morphinics in DM1

# THE RESPIRATORY CARE RECOMMENDATIONS

# General Considerations: why?

- Make patients proactive for better care
  - Provide non-specialists with clear indications as to what to do
- Standardize treatment protocols and procedures to minimize the risks of unequally distributed SoC in preparation for clinical trials

# The Respiratory Care Recommendations

---

MDF recruited x international experts in DM and in respiratory and sleep medicine

Two-phased blended consensus-building methodology using the Single Text Procedure

The single document incorporated the input and contributions of stakeholders with a consensus-building approach

The draft document was circulated to Working Group members and MDF aggregated all the revisions and suggestions into a single updated document

Recommendations in conflict were paired and provided to the group for discussion through serial conference calls

# The Respiratory Care Recommendations

---

➤ LOOK FOR

➤ TEST FOR

➤ TREAT WITH



LOOK FOR



# LOOK FOR: Respiratory symptoms

Respiratory symptoms that may indicate:

- i. nocturnal hypoventilation** (poor sleep, morning headaches, orthopnea, excessive daytime sleepiness);
- ii. obstructive sleep apnea** (snoring, apnea, poor sleep, orthopnea, excessive daytime sleepiness)
- iii. decreased respiratory reserve** or decreasing pulmonary function (dyspnea, fatigue, shortness of breath, decreased exercise tolerance);
- iv. Ineffective cough** (decreased ability to cough, coughing when eating or drinking, choking, history, frequency and duration of chest infections including hospitalizations)

# LOOK FOR: Respiratory muscle use

## **Pulmonary exam must include at minimum:**

- resting respiratory rate
- pulse oximetry
- Auscultation
- assessment of chest wall motion
- evaluation of use of accessory muscles
- recruitment of abdominal muscles and breathing pattern
- Are there signs of diaphragmatic paralysis?
- When lying flat is there orthopnea / tachypnea or paradoxically breathing
- Ask the patient to cough and check strength of cough

# What else can I expect during a pulmonary visit?

---

- Discuss respiratory tests
- Discuss respiratory treatments
- Discuss advanced directives
- Discuss research



TEST FOR

# TEST FOR: FVC and FEV1

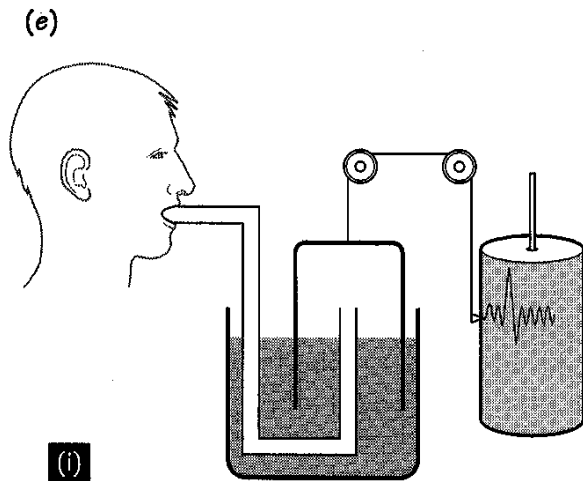
Forced vital capacity (FVC) and forced expiratory volume in one second (FEV1) in the sitting and supine positions if possible, every 6 months.

Spirometry test should be performed with either a mask or mouthpiece; in the case of weakness of orbicularis oris muscle. In either instance the device that provides the better fit should enable a more precise measurement.

FVC value is considered abnormal if less than 50% of predicted normal value, or if it falls by more than 20% or more than 500 ml from sitting to supine.



# Spirometry: The Forced Vital Capacity (FVC)



(i)

water filled spirometer

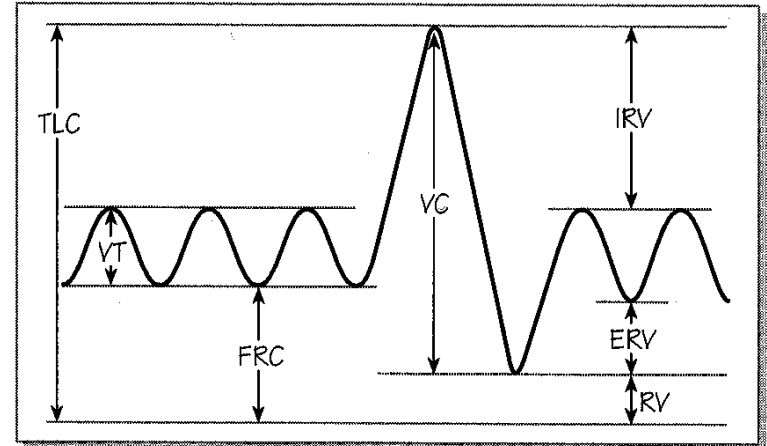


Table 1

Tidal volume (VT) (at rest)	500 mL	Total lung capacity (TLC)	7300 mL
Vital capacity (VC)	5500 mL	Functional residual capacity (FRC)	3500 mL
Inspiratory reserve volume (IRV)	3300 mL	Residual volume (RV)	1800 mL
Expiratory reserve volume (ERV)	1700 mL		

**FVC is Usually Reported as  
% Predicted Value**

# Pitfalls of Pulmonary Testing

- Tests require a tight seal around a mouthpiece
- Weakness of facial muscles in DM can be a problem



# TEST FOR: respiratory muscle strength

Respiratory muscle strength evaluation with the maximum inspiratory pressure (MIP) and maximum expiratory pressure (MEP) in the upright position, every 6 months.

MIP value is considered abnormal if less than 60 cmH<sub>2</sub>O, MEP if less than 40 cmH<sub>2</sub>O. In children, normal MIP and MEP values change according to size of the child.

Sniff nasal inspiratory pressure (SNIP) testing can be used if the patient is unable to tolerate the MIP due to myotonia or other mitigating symptoms).





# TEST FOR: peak cough expiratory flow

- Measure PEF during cough with a spirometer or with PEF specific device



Normal range:

- 360-1000 l/min (Bach,1993)

Cough is ineffective when:

- PCF < 160 l/min (Bach, 1996)
- PCF **160 l/min-270 l/min**: patients at risk during infections or peri-operatively (Mier-Jedrzejowicz, 1988)
- VC < 1.5 L (Bach, 1993)
- PE max < 60 cmH<sub>2</sub>O (Miske, 2004)

# TEST FOR: peak cough expiratory flow

Cough peak expiratory flow, every 6 months.

If PCEF is less than 270 liters/minute then cough is considered ineffective, and manually and/or mechanically cough assistance techniques should be implemented.



# Cough

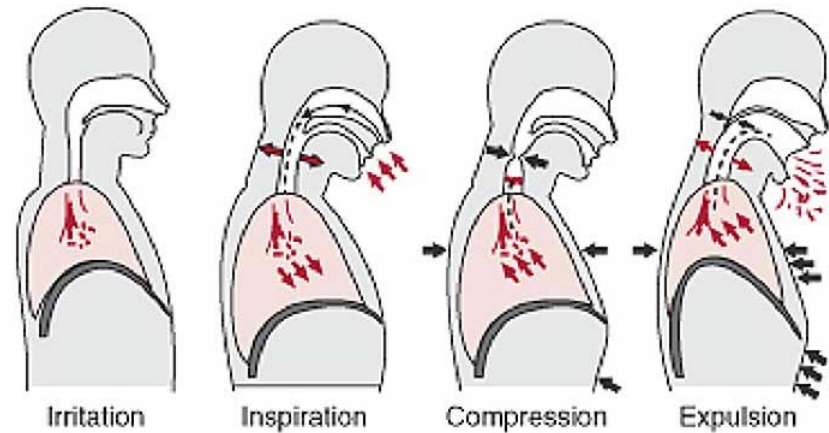
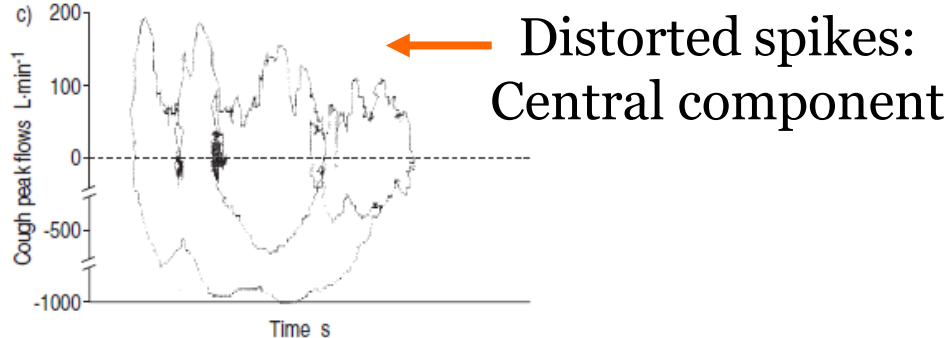
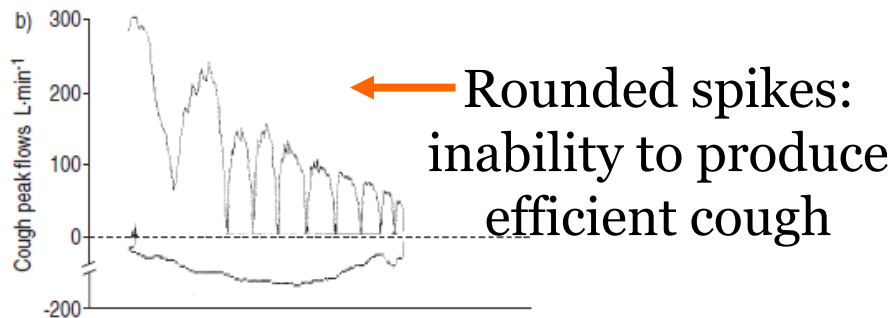
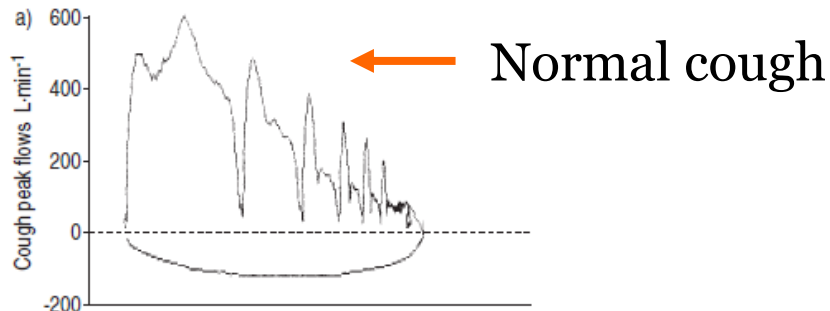


Fig. 1. – a) A series of cough spikes superimposed on the maximal expiratory flow volume curve. b) An example of a patient who was unable to produce cough spikes. c) A grossly distorted cough flow/volume curve in a bulbar patient.

# PCF and extubation or decannulation

---

- PCF of at least 160 L/min is necessary for the successful extubation or tracheostomy tube decannulation of patients with neuromuscular disease

# Chest X-rays

Look for:

- Infections or other lung problem
- Asymmetrical diaphragm elevation
- Abnormal cardiac image



# TEST FOR: nocturnal oxymetry

Nocturnal oximetry /capnography or polysomnography, every 6 months.

This test is considered abnormal if Oxygen Desaturation Index (ODI) is greater than 15/hour. ODI reveals oxygen levels drop during apneas (desaturations)



# TEST FOR: arterial blood gases

Arterial Blood Gases (ABGs) or capnography.

Adaptation to noninvasive ventilation (NIV) should be considered if  $p\text{CO}_2$  is greater than 45 mmHg (6.0 kPa).



After a pulse is found, a blood sample is taken from the artery

# TEST FOR: sleep disordered breathing

## Sleep Related Breathing Disorders (SRBD)

### Common Physical Findings

- Enlarged tongue
- Overweight/obesity
- Enlarged tonsils and/or uvula
- Small lower jaw/retruded chin
- Nasal polyps/congestion

### Common Signs & Symptoms

- Snoring
- Irritability
- Personality changes
- Depression
- Excessive daytime sleepiness
- Poor memory/confusion
- Night time sweating
- Decreased sex drive/loss of intimacy
- Diminished performance
- Accident proneness
- Morning headache
- Irritant to bed partner
- High blood pressure
- Diabetes
- Stomach acid regurgitation

© 2012 Dear Doctor, Inc.

Signs of sleep-disordered breathing including snoring, apneas, nightly interrupted or fragmented sleep.

MIP values of less than 60 or an FVC of less than 50 percent of predicted via an in laboratory sleep study or other respiratory test.

If DM1 patients have sleep disorder symptoms such as excessive daytime sleepiness, fatigue, morning headaches and poor sleep, the patients should be evaluated with a sleep study.



Normal airway

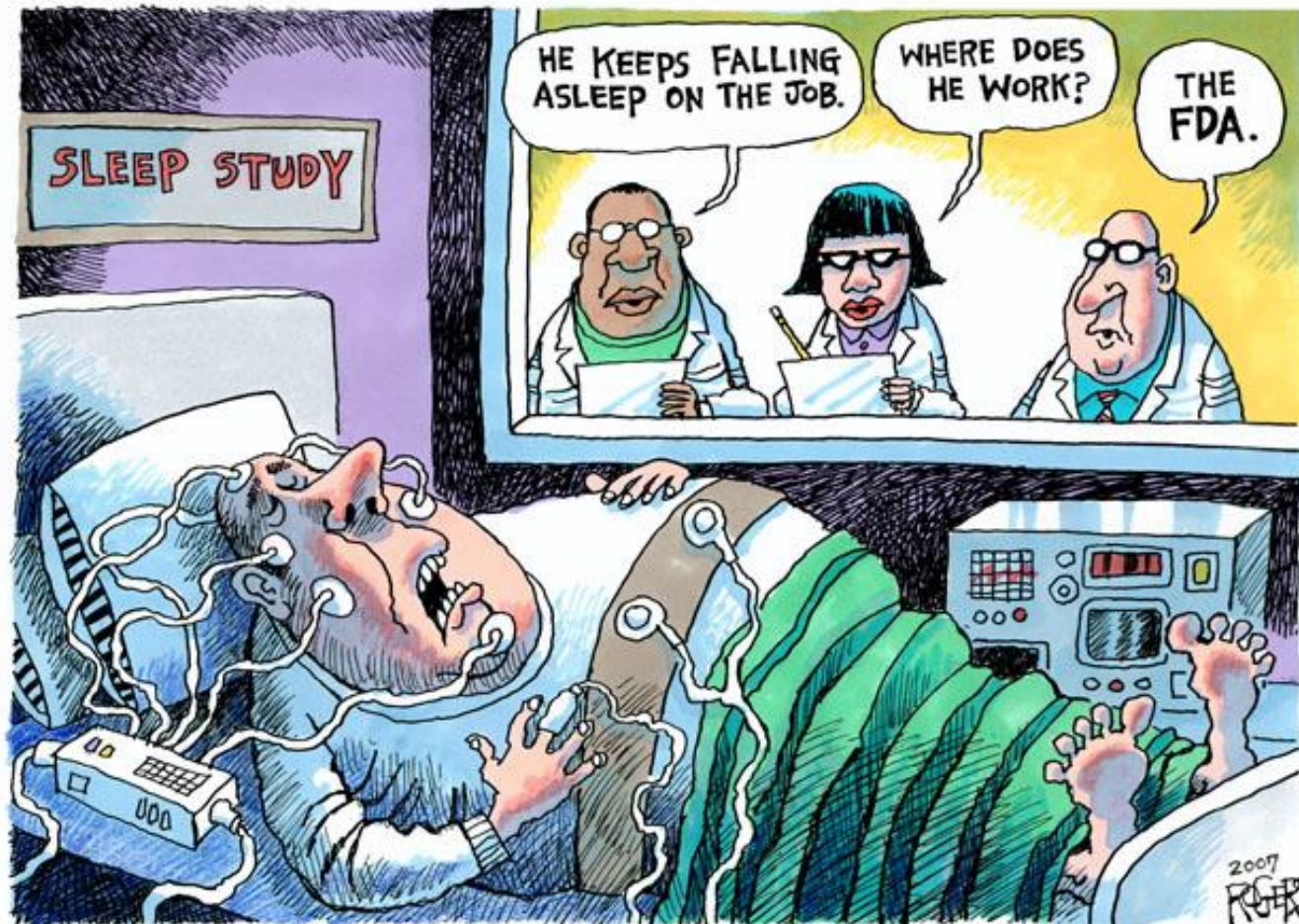
Obstructive sleep apnea



# Sleep study

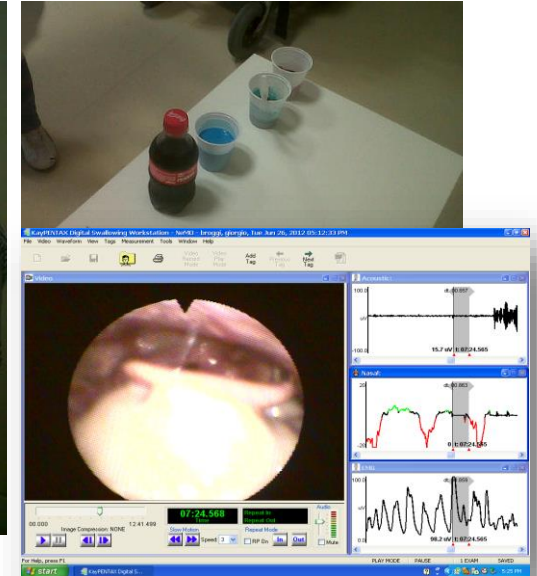
SECOND OPINION

BY ROB ROGERS

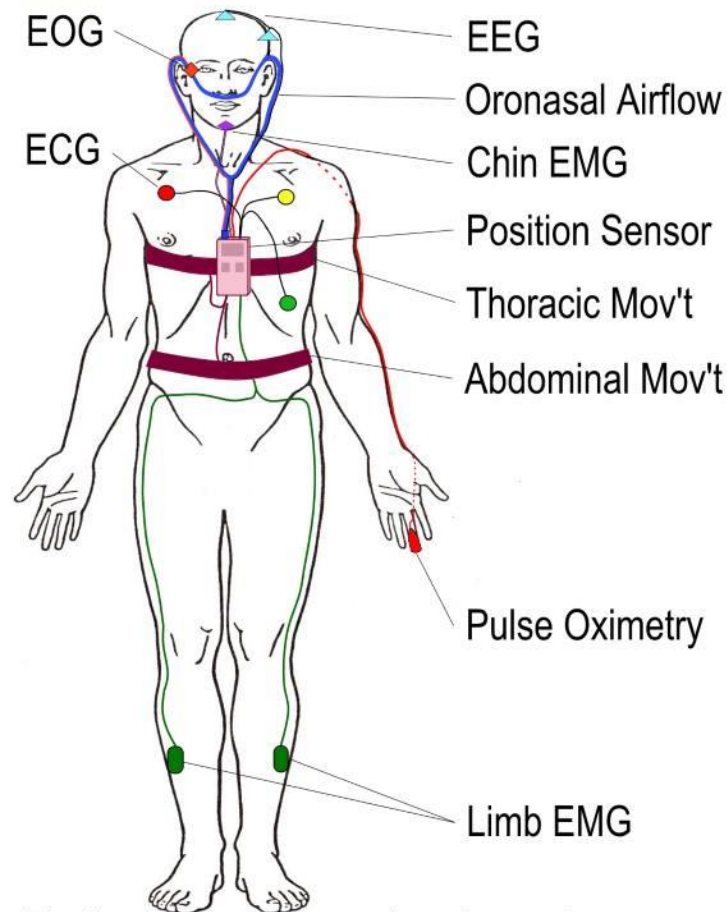


# TEST FOR: swallowing

Patient should be referred to a specialist in dysphagia evaluation if swallowing problems are suspected (cough before, during or after meals, food stagnation in the oral cavity, drooling, regurgitation of undigested food, aspiration, gurgling in the throat, dysphonia, malnutrition).

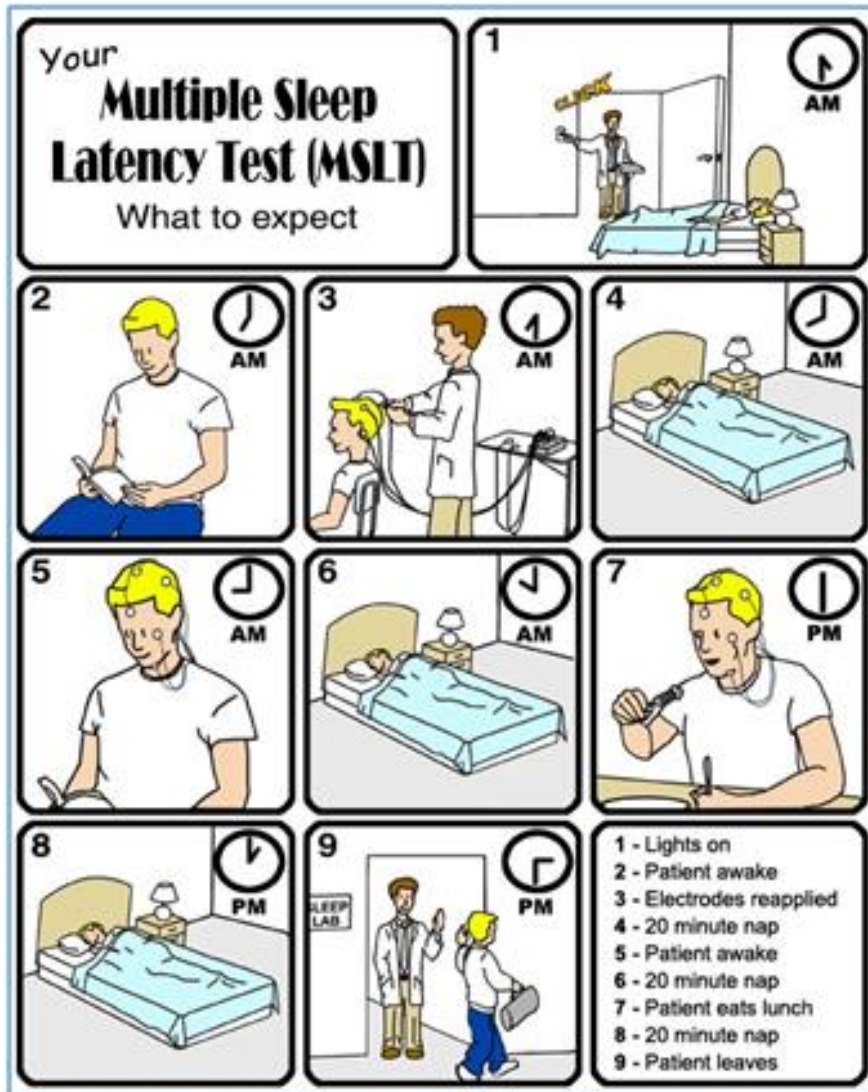


# Polysomnography (PSG)



Polysomnography Leads

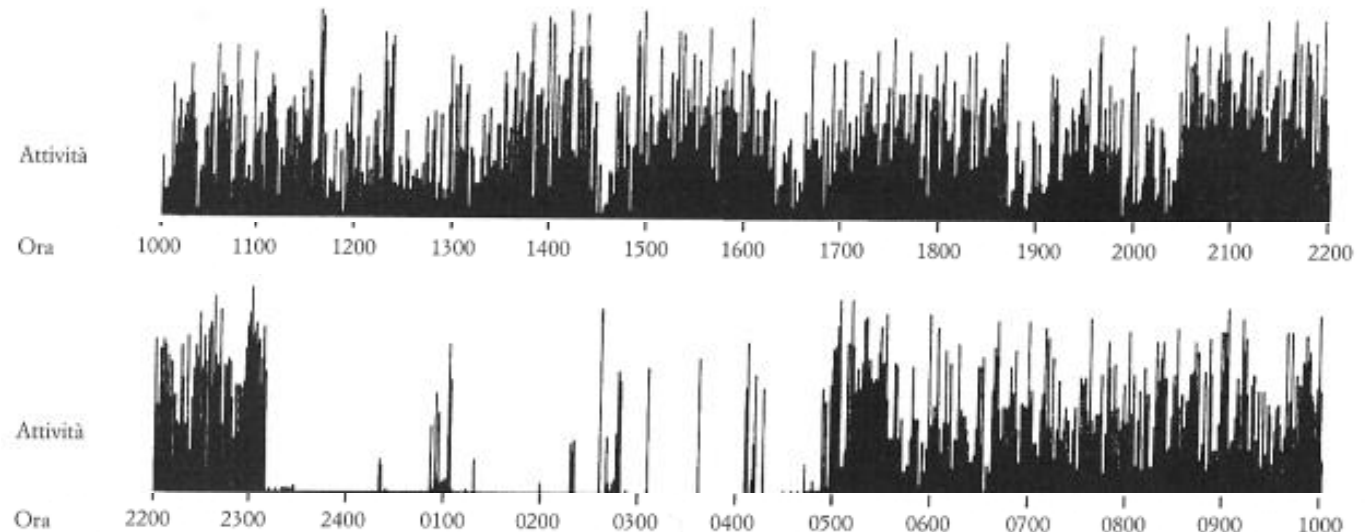
# Multiple sleep latency test



Positive if mean latency to fall asleep is  $< 8$  minutes

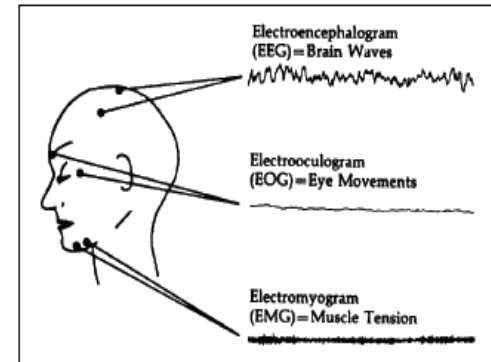
# Actigraphy

Actigraphy is a non-invasive method of monitoring human rest/activity cycles.



# Maintenance of wakefulness test (MWT)

- Tests the ability of the patient to stay awake
- 4 sessions each 40 minutes long





# TAKE-HOME MESSAGES

# Summary

- Breathing involvement in DM is highly variable
- Weakness of inspiratory and expiratory muscles is common
- Illness and death due to breathing complications occurs
- Oxygen can cause problems – be cautious
- Routine pulmonary evaluation is important
- Treatment may include non pharmacological approaches with BiPAP, assisted cough and pharmacological approaches with modafinil if EDS is documented to be of central origin



# THANK YOU!!

