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Mechanical insufflation-exsufflation for cough augmentation in neuromuscular disease: a physiological approach

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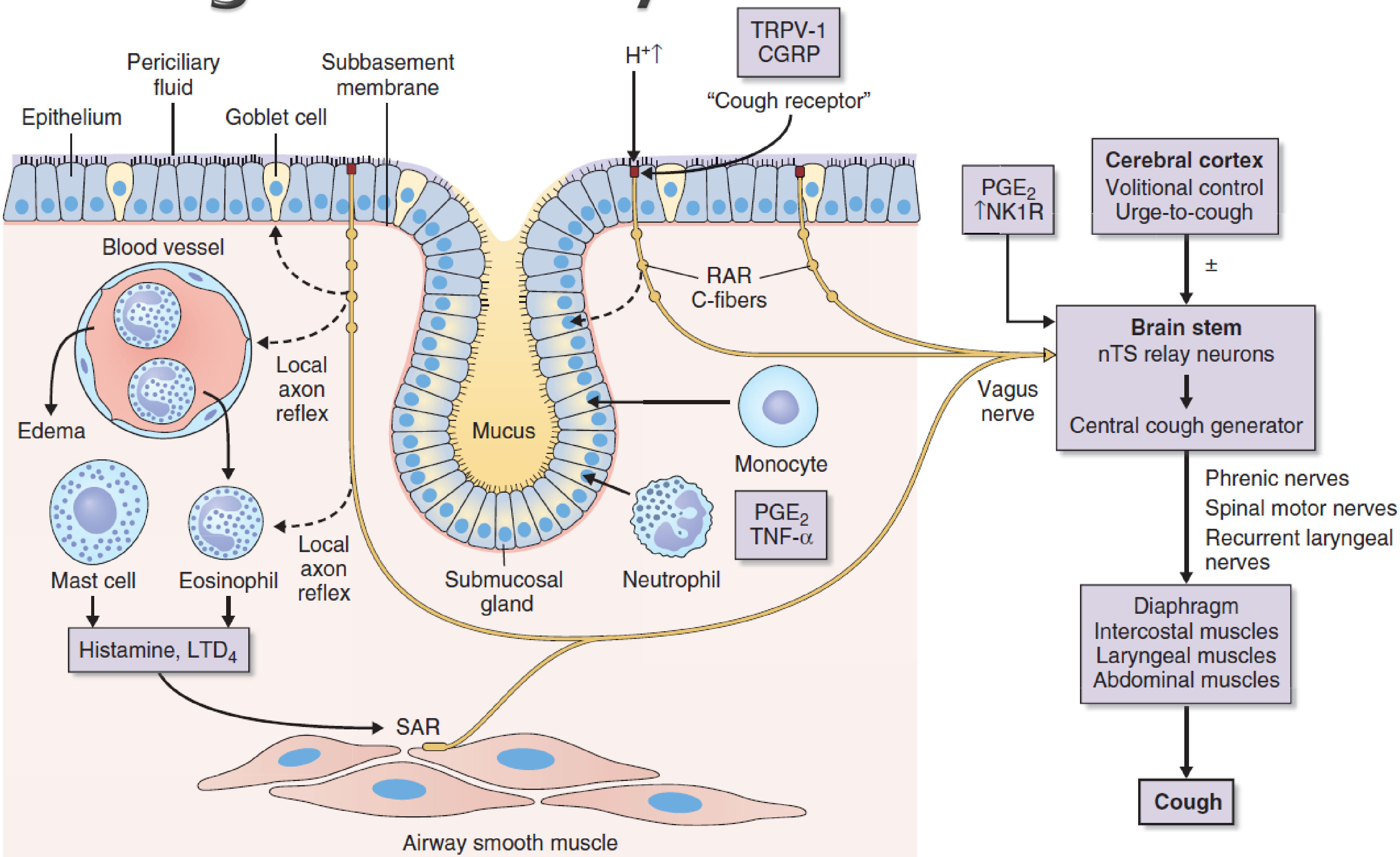
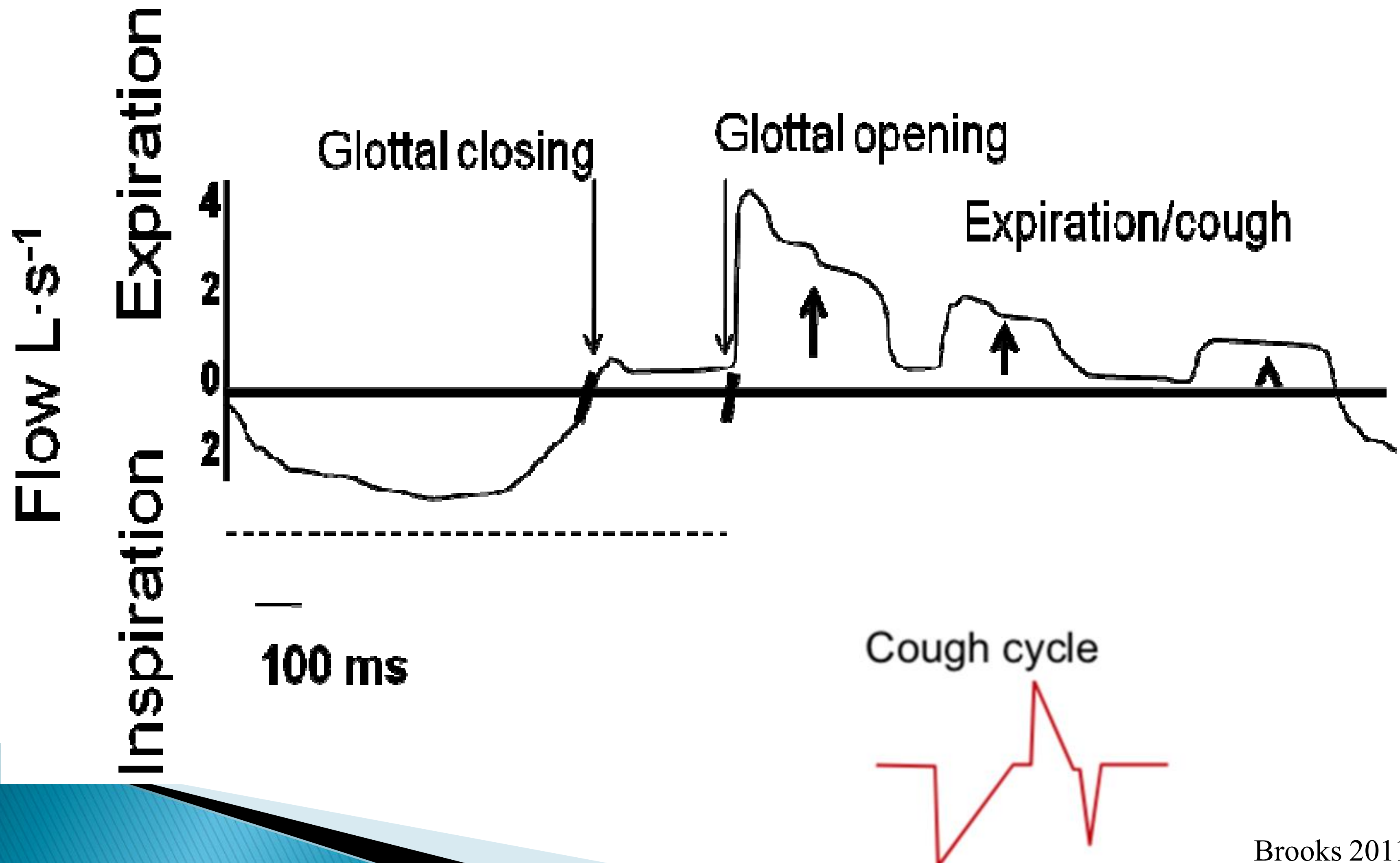
Cough Pathway



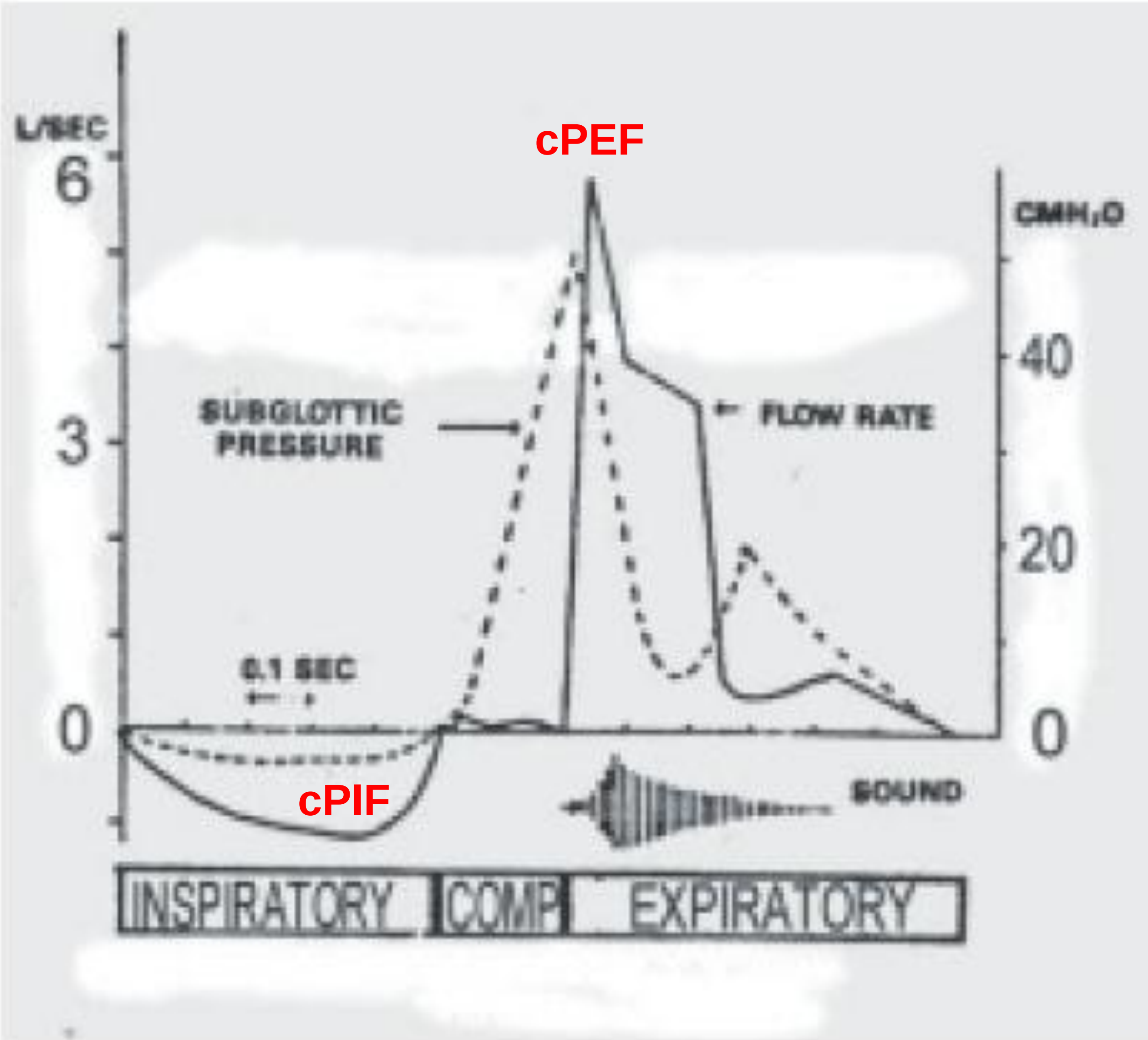
Birring and Pavord 2012

Phases of normal cough cycle



Brooks 2011

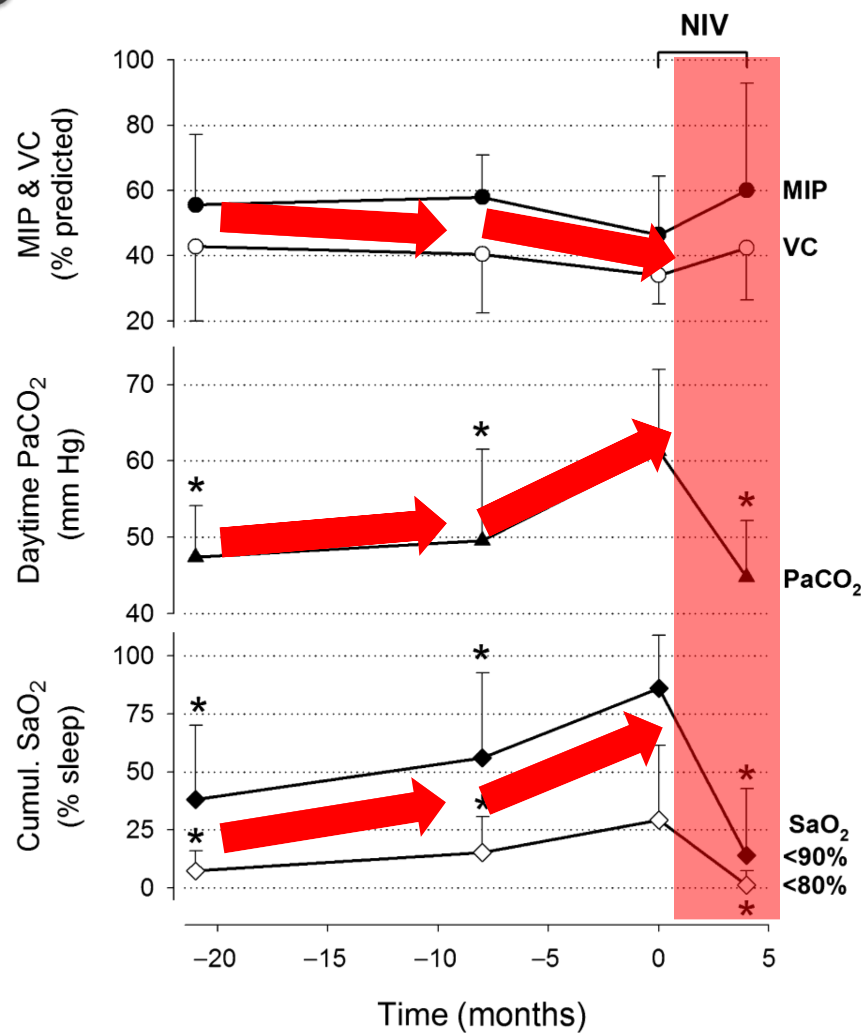
Phases of normal cough cycle



Brooks 2006

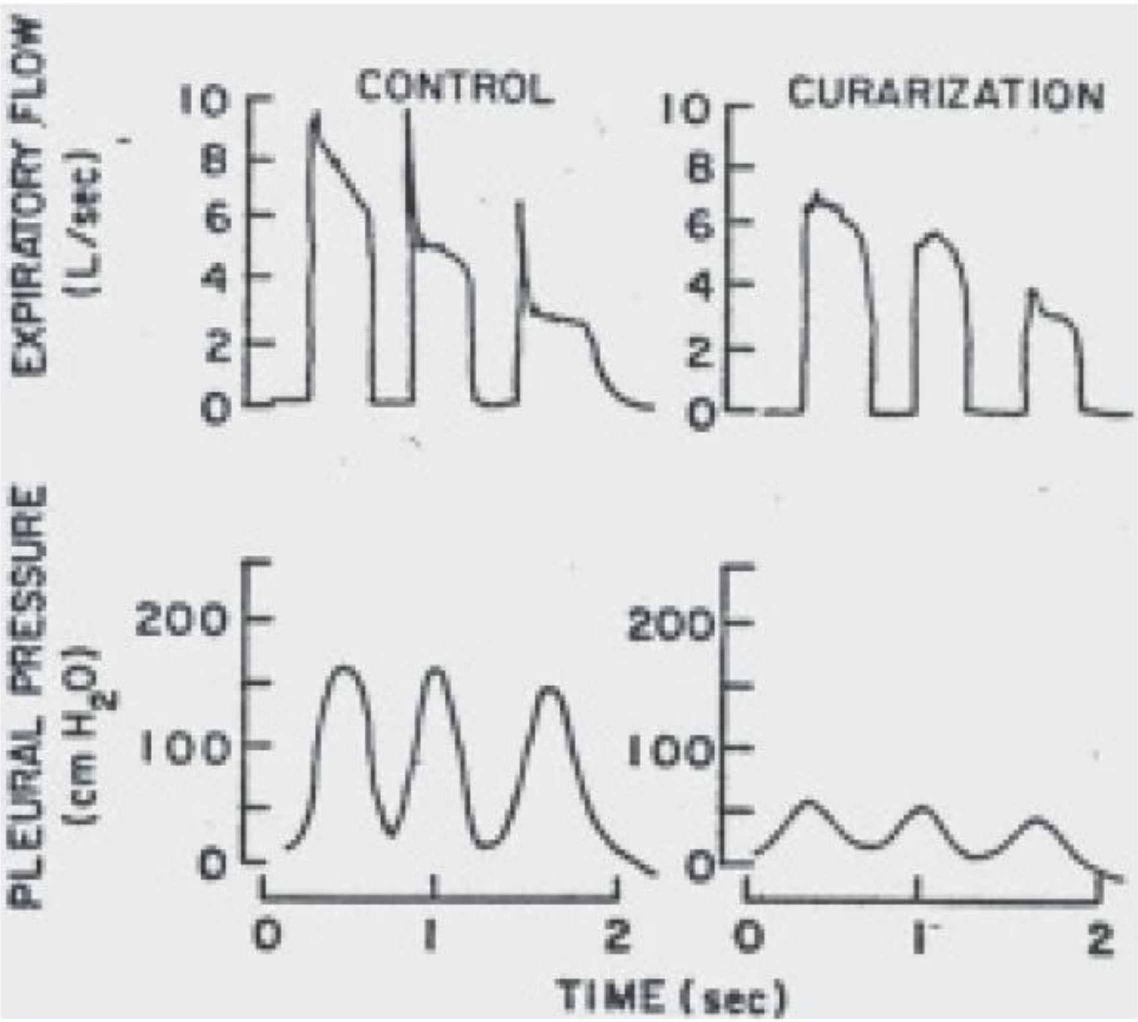
Progression of respiratory muscle weakness in NMD

- Muscular dystrophies
  - Duchenne
  - Becker
  - Fascio-scapular-humeral
  - Limb girdle
- Polio
- ALS



Hillman D, et al. Respirology 2014; 19: 1106-1116

Expiratory pressure and flow



Inhaling to high lung volumes
+
Glottic closure

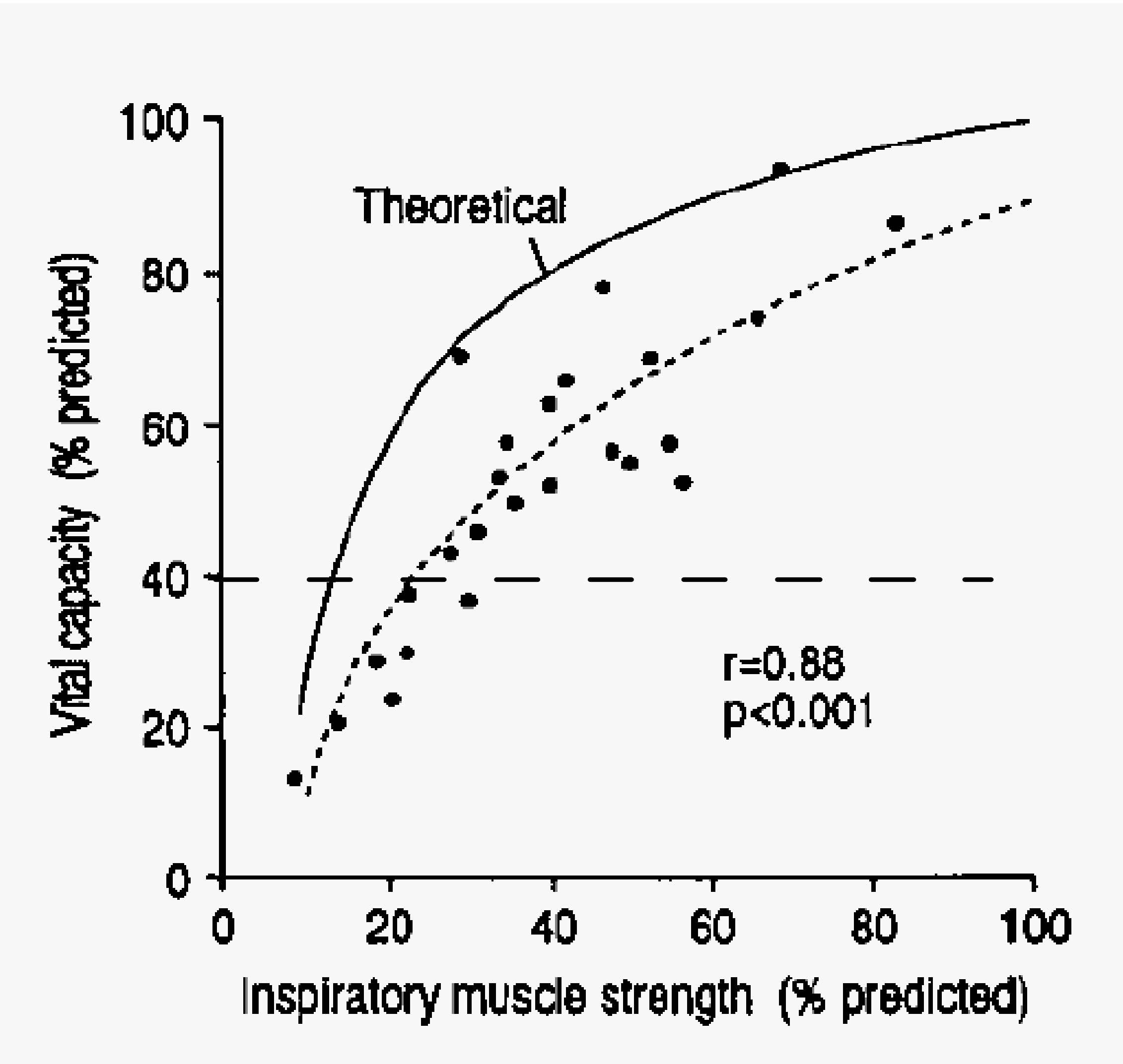
High intrathoracic pressures

-Provide the driving force for airstream flow during cough

-Dynamically compress the central airways, which further enhances the cough airstream velocity

Arora 1981

Volume Pressure Relationship

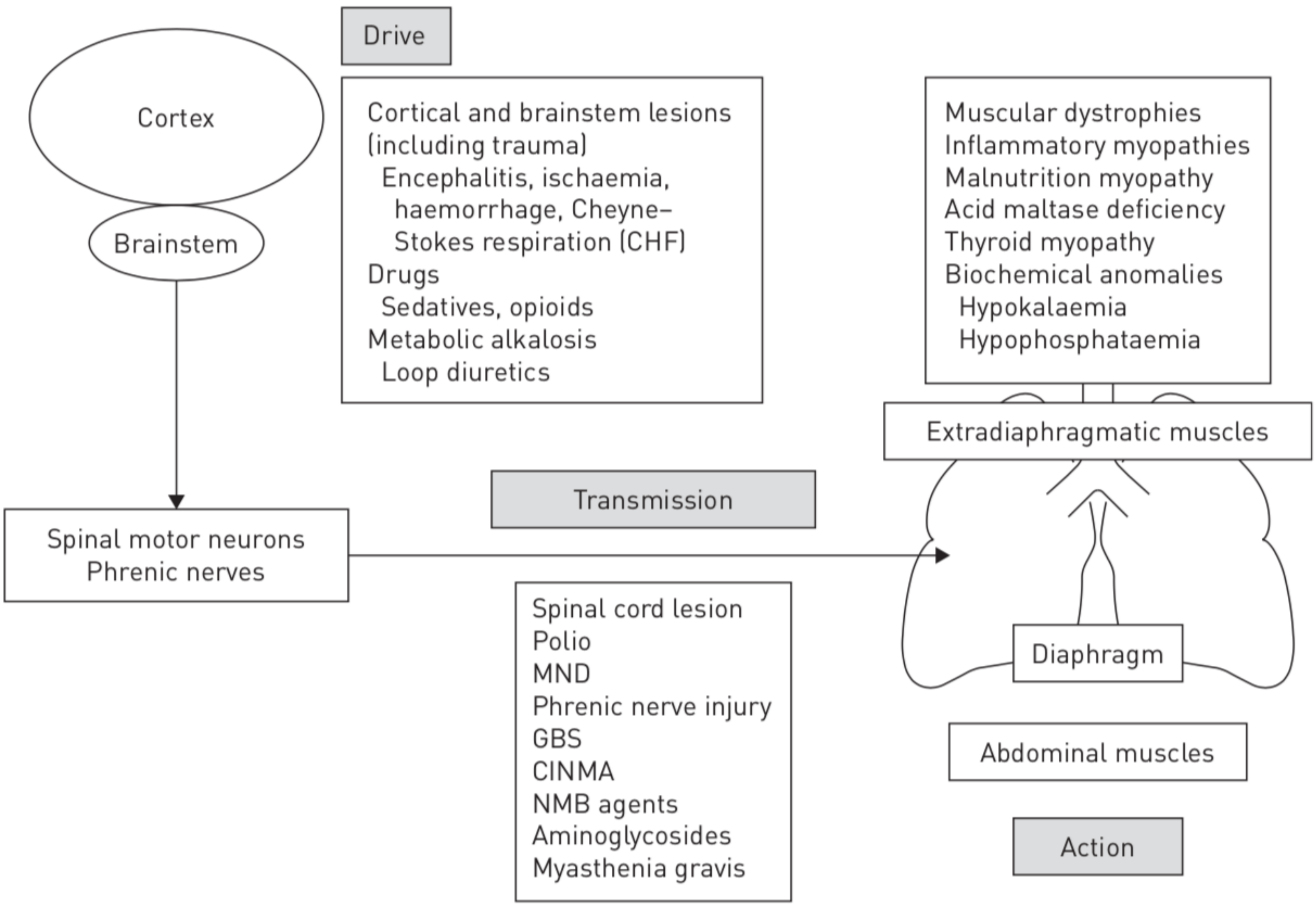


Curvilinear relation

Maximum
Static Inspiratory Pressure
to
Vital Capacity

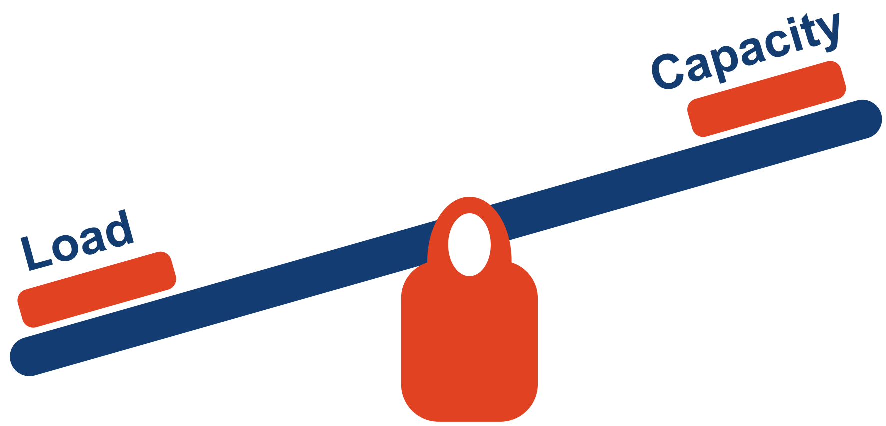
Detroyer A, et al.Thorax 1980; 35: 603-610

Respiratory Muscle Pump



Cough Function

Presence of excessive bronchial secretions

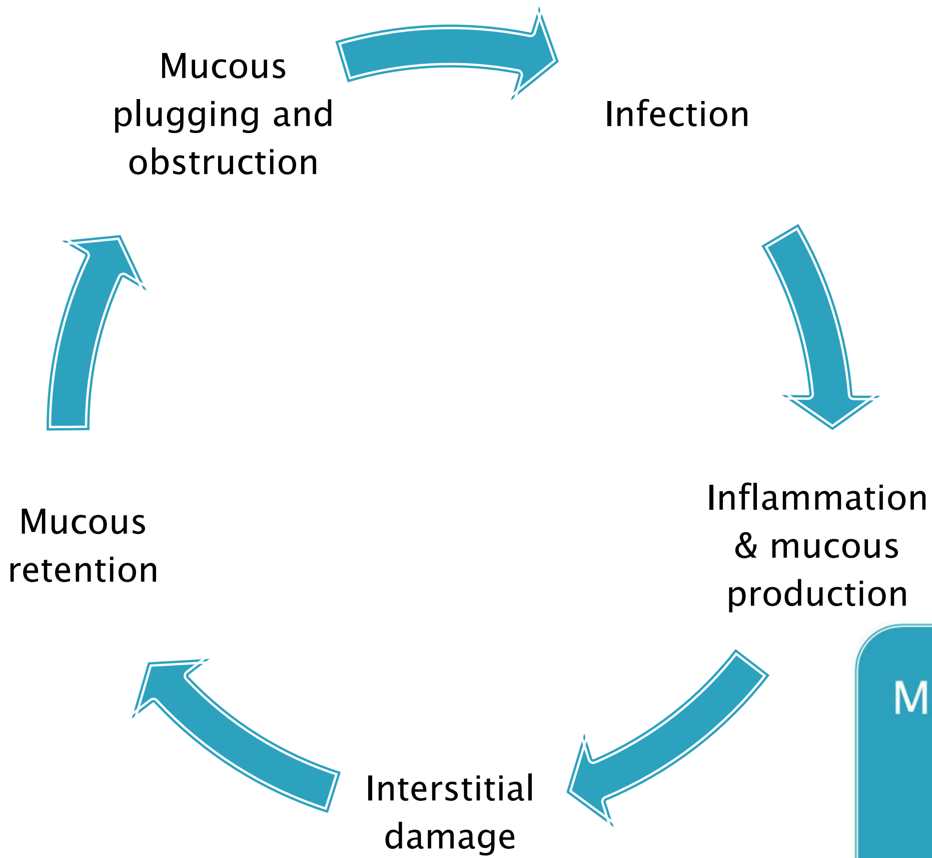


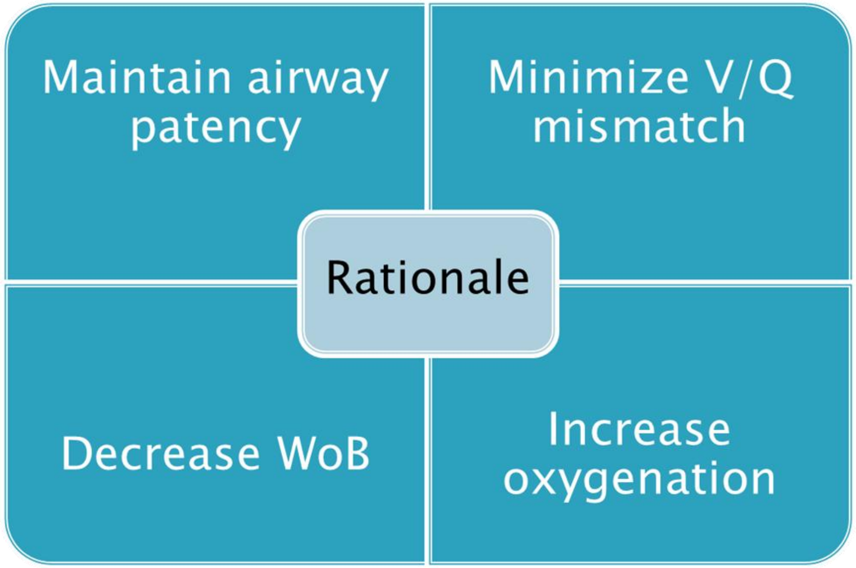
Cough Pathway

Respiratory Muscle Pump

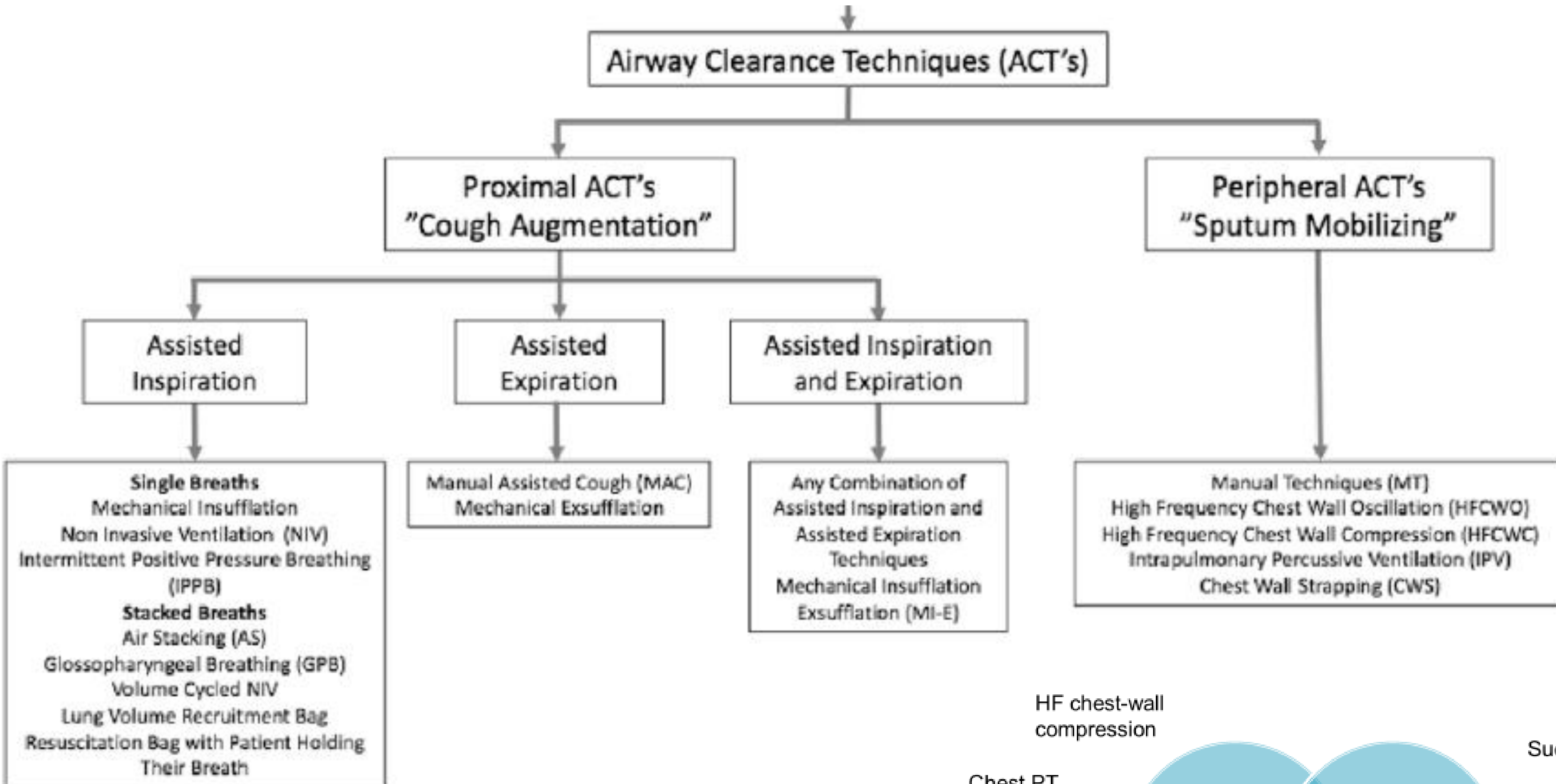
Bulbar, Glottis, and Vocal Cord Function

Complications of Retained Secretions

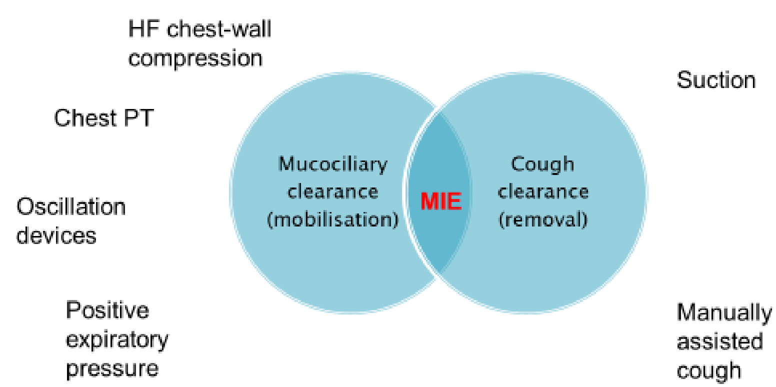




Airway Clearance Techniques



Chatwin 2018



Mechanical Insufflation:Exsufflation

- Positive pressure to airway
- Rapid shift to negative pressure – produce high expiratory flow rate
- Delivered via Face Mask, Tracheostomy or endotracheal tube

Cough Assist T70

CA3000 Device

Vital Cough System

Clearway

Pegaso

Manual/Auto control

Allows you to choose whether you want to switch the pressures automatically or manually.

Pressure gauge

Reads the pressure during inhalation and exhalation.

Inhale

Determines how long the positive pressure will be blowing into the lungs.

Manual lever

Allows you to toggle between inhale and exhale when using the manual setting. This control also allows you to set and check your pressures.

Exhale

Determines how long the negative pressure will be forcing air out of the lungs.

Inhale pressure

Determines the amount of positive pressure that will be blowing into your lungs.

Pause

Determines the time between inhalation and exhalation.

Inhale flow

Sets the amount of flow needed during inhalation. There are two settings: Full or Reduced.

Power

Allows you to turn power on (I symbol) and turn power off (0 symbol).

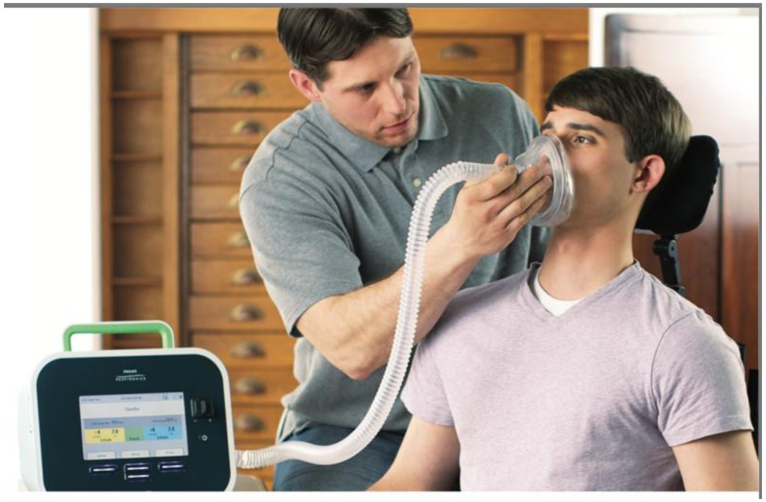
Pressure

Determines the amount of negative pressure that will pull air out of your lungs.

- **Parameters that can be adjusted:**
  - **Insufflation and Exsufflation pressure**
  - **Inspiratory and expiratory time**
  - **Inspiratory rise time**
  - **Pause**
  - **Oscillations**

Indications

- Ineffective cough due to NMD
- Ineffective cough due to respiratory muscle fatigue



Contraindications

- Bullous emphysema
- PTX / Pneumomediastinum
- Recent barotrauma
- Haemoptysis

Avoid Intubation
Facilitate Extubation and decannulation
Prevent post-extubation failure

Efficacy

- NMD patients:
  - cPEF increases significantly with MI-E (Bach 1993) – when stable (Stehling 2015) and during LRTI (Jung 2018)
  - Superior to other secretion clearance techniques (Chatwin 2003, Kim 2016)
  - Improves mechanics (Cesareo 2018; Nunes 2019)

- Bulbar weakness patients – less of an improvement in cPEF (Mustfa 2003, Sancho 2004)

- Improves oxygenation and breathlessness scores (Winck 2004)
- Reduced need for intubation/tracheostomy during LRTI (Vianello 2005)
- Shorter time spent on secretion clearance (Chatwin 2009)

However…

- Tolerance variable
- Physiology poorly understood
- Limited RCTs to advise on management – higher pressures, flow bias
- Multiple possible parameters (Pressure, Rise Time, Ti/Te)

Aim

To assess the effect of different insufflation and exsufflation pressures on physiological outcomes

Material and Methods

- Patients with:

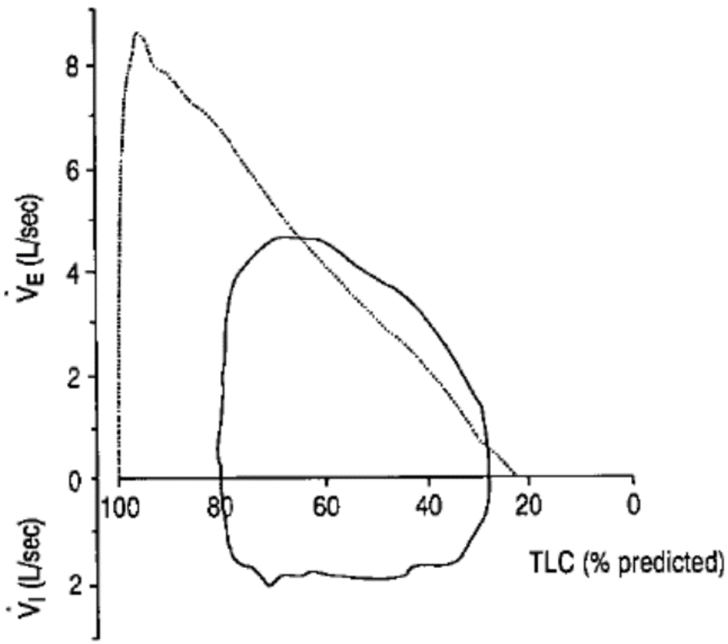
–Neuromuscular disease

–Respiratory muscle weakness

–History of recurrent respiratory secretions or infections established on cough augmentation with MIE

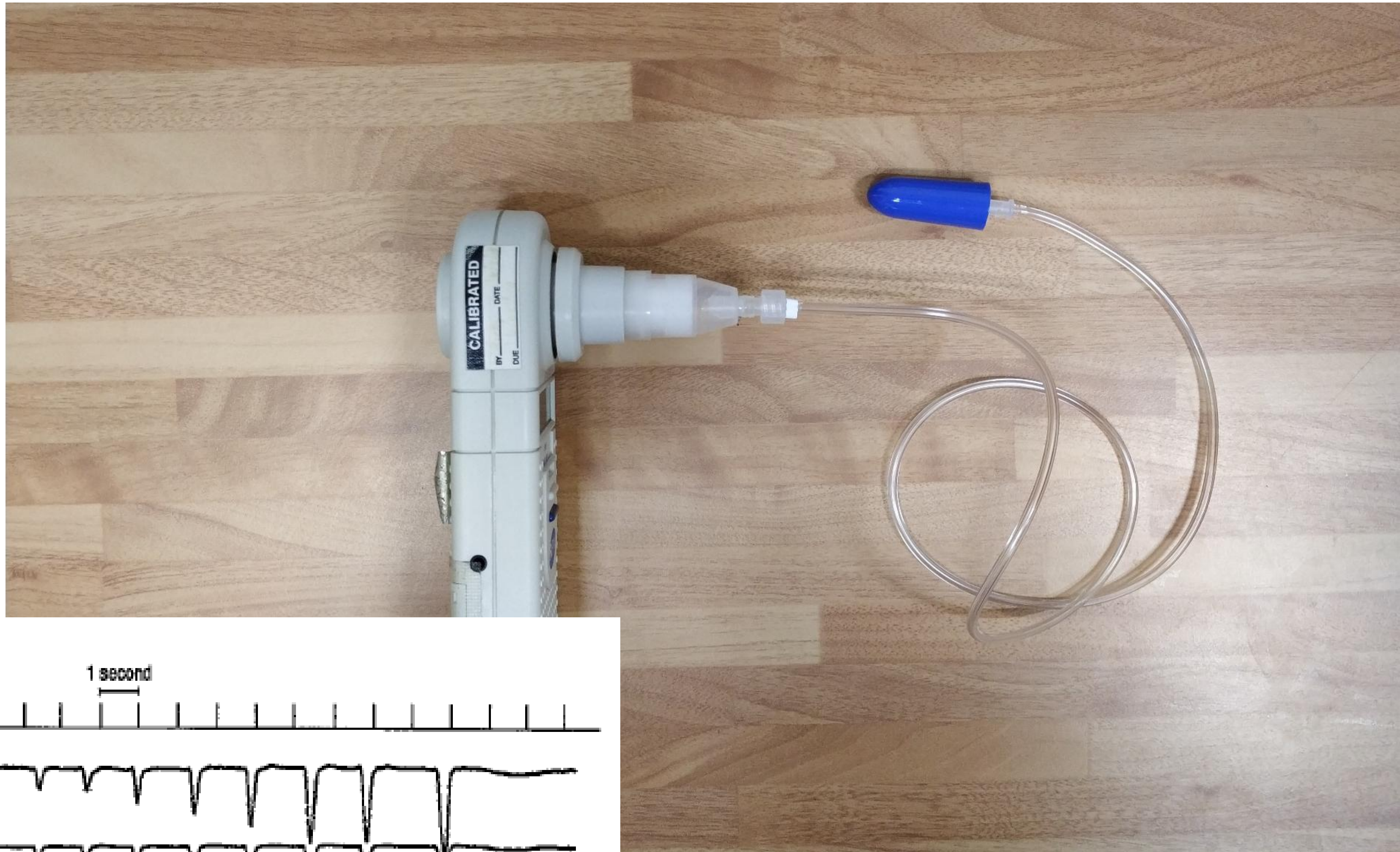
- Clinically stable for 4 weeks

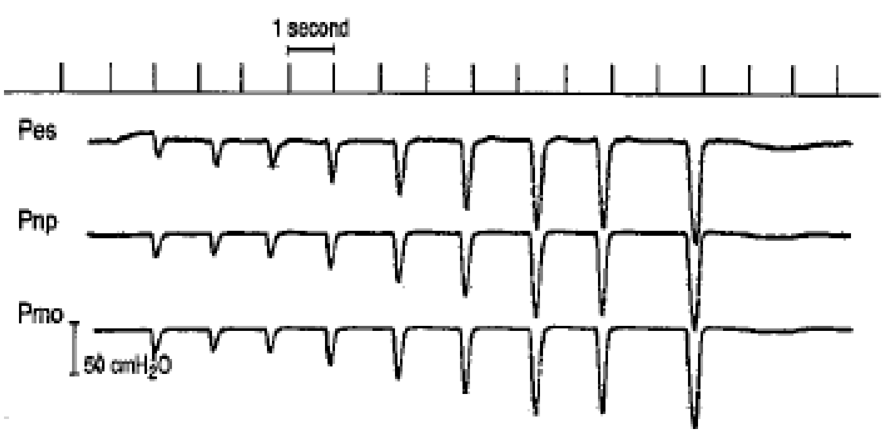
Spirometry and cPEF



Tests	Main variables	Reference values and discriminative values	Repeatability / reliability / validity	Cautions	Setting (expert centres, general clinical use, research…)	Remarks
				complementary and not interchangeable in the evaluation of inspiratory weakness		
	PCF	Healthy subjects: 468-588 l·min^{-1} [301] Increased extubation / weaning failure <160 l·min^{-1} in NMD patients [302]	No sufficient data available	At least 3-6 PCF with <5% variability need to be assessed [17]	Simple to be assessed Especially useful in NMD patients	No direct link between "cut off" values and clinical consequences (e.g. cough assist, etc.).

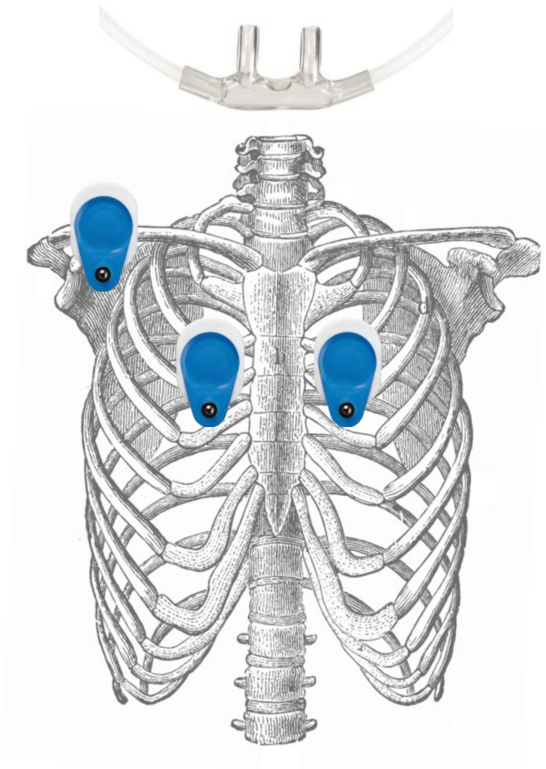
Respiratory Muscle Function

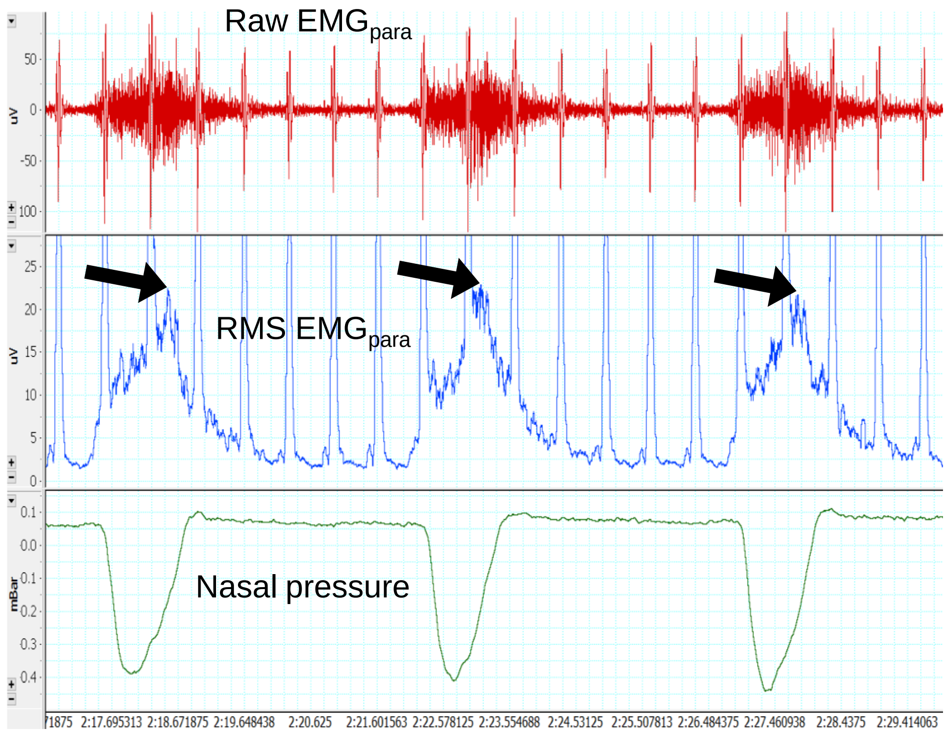


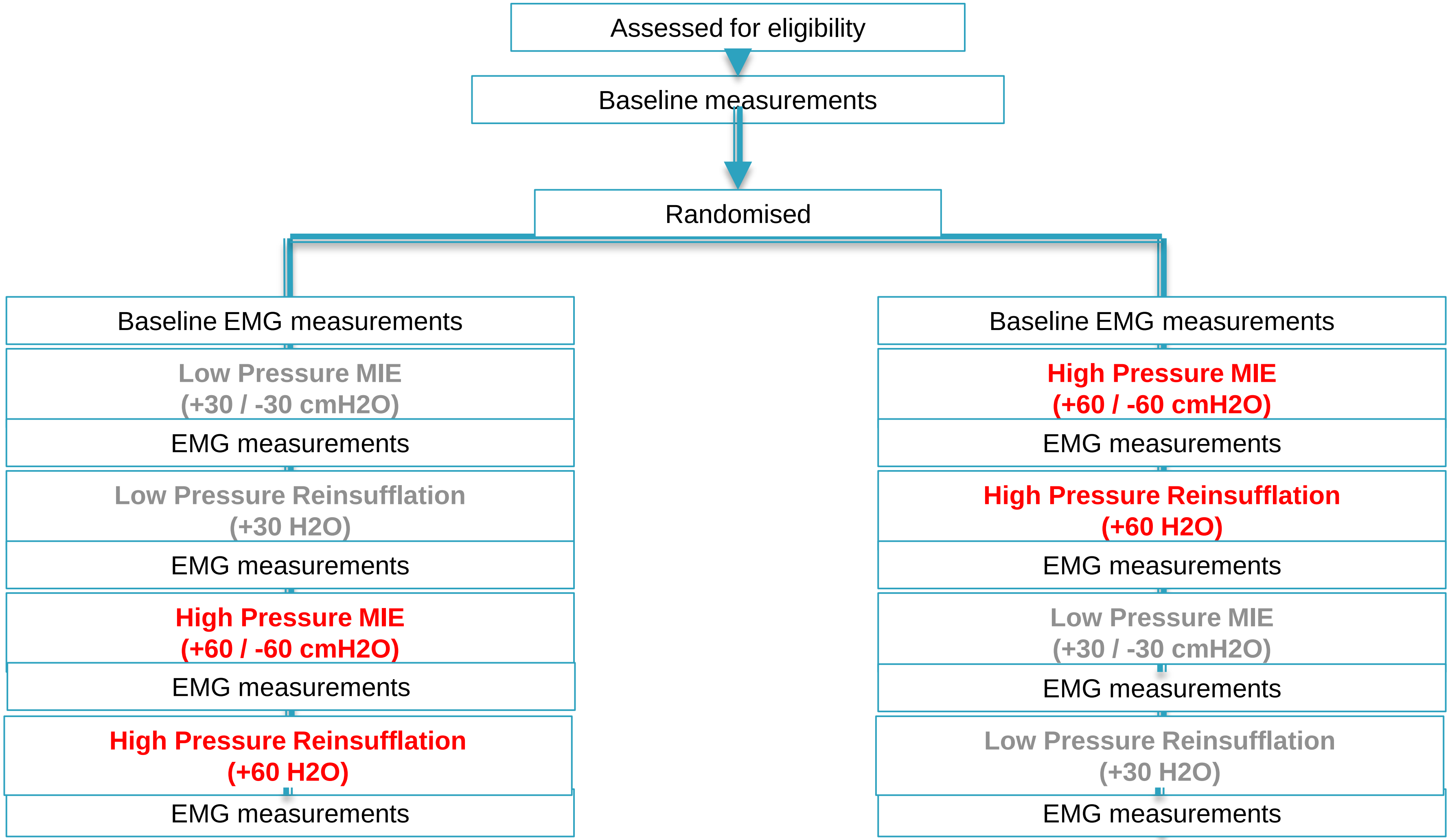


Koulouris N, Vianna LG, Mulvey DA, Green M, Moxham J. Maximal relaxation rates of esophageal, nose, and mouth pressures during a sniff reflect inspiratory muscle fatigue. *Am Rev Respir Dis* 1989;139: 1213–1217.

Parasternal Electromyography



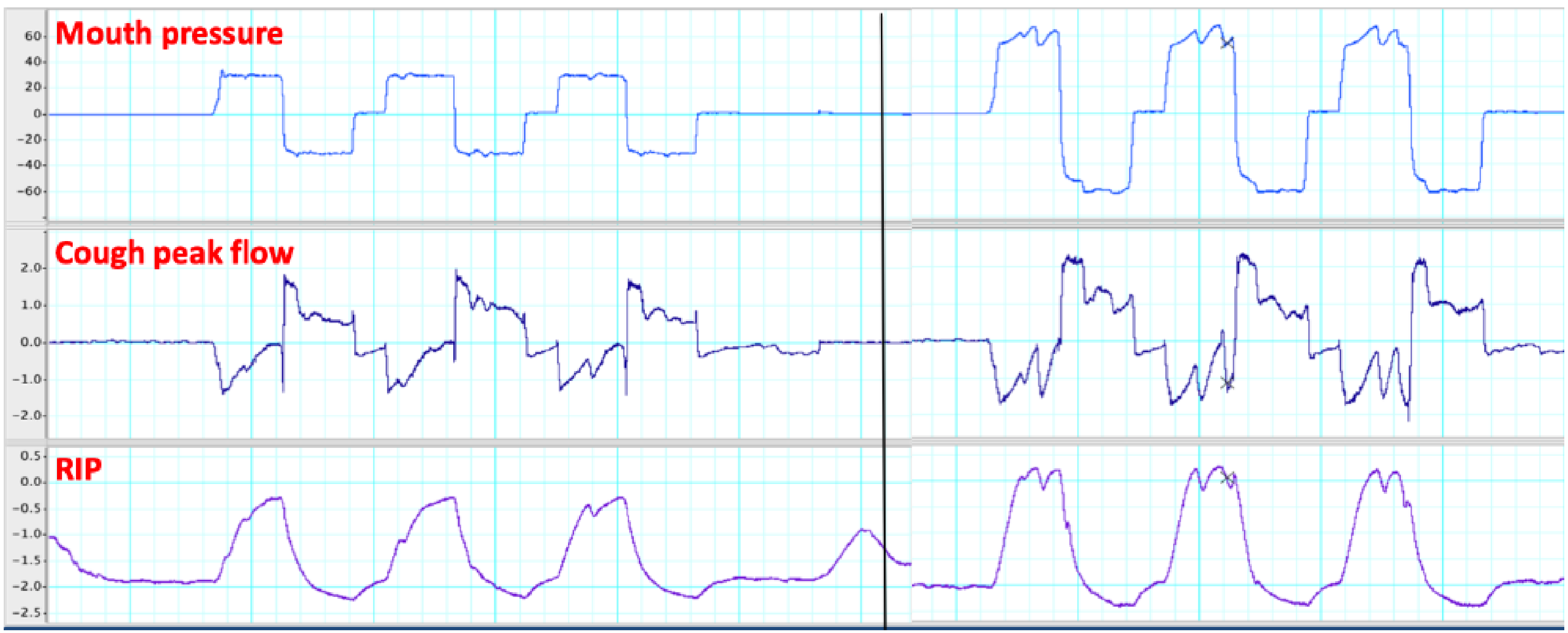



Assessed for eligibility
Baseline measurements
Randomised
Baseline EMG measurements
Low Pressure MIE
(+30 / -30 cmH2O)
EMG measurements
Low Pressure Reinsufflation
(+30 H2O)
EMG measurements
High Pressure MIE
(+60 / -60 cmH2O)
EMG measurements
High Pressure Reinsufflation
(+60 H2O)
EMG measurements
Baseline EMG measurements
High Pressure MIE
(+60 / -60 cmH2O)
EMG measurements
High Pressure Reinsufflation
(+60 H2O)
EMG measurements
Low Pressure MIE
(+30 / -30 cmH2O)
EMG measurements
Low Pressure Reinsufflation
(+30 H2O)
EMG measurements

Results

+30/-30cmH2O

+60/-60cmH2O



Results

	DMD (n=10)	LTTV (n=11)	SCI (n=8)	P-value
Age (years)	26.9 ± 4.3*†	49.6 ± 20.5*	54.3 ± 19.1†	0.002
Gender (male/female)	10	10	4	–
Percutaneous endoscopic gastrotomy (PEG) feeding (Y/N)	6/4	8/3	0/8	–
Domiciliary insufflation pressure (cmH_2O)	39.4 ± 5.8	37.3 ± 7.5	37.1 ± 8.1	ns
Domiciliary exsufflation pressure (cmH_2O)	–53.3 ± 6.1	–45.7 ± 8.4	–51.3 ± 7.5	ns
Tolerated high pressure protocol (%)	40	87.5	73	–

Results

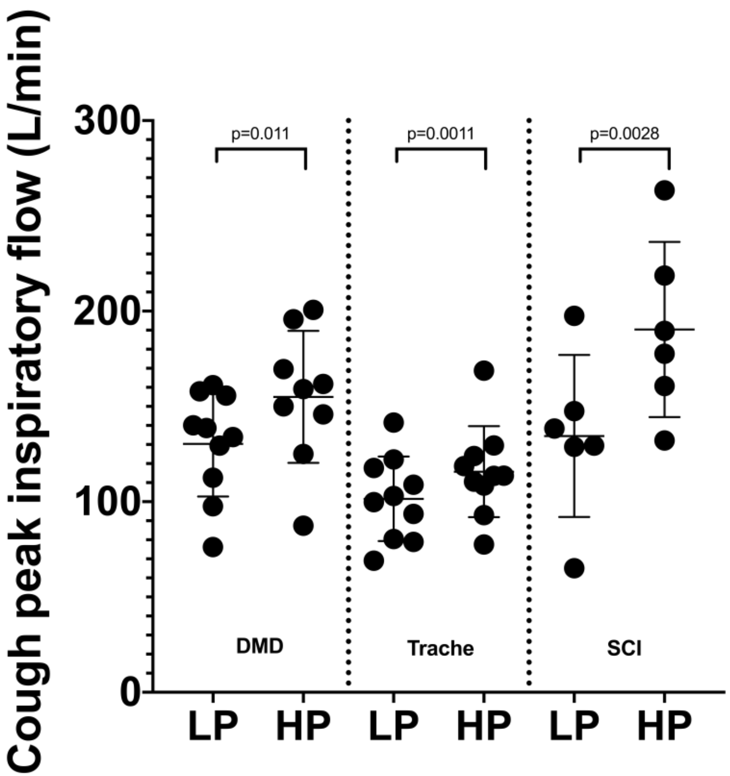
	DMD (n=10)	LTTV (n=11)	SCI (n=8)	P value
Minute ventilation (L/min)	5.7 ± 1.9	7.0 ± 0.6	8.5 ± 3.0	ns
Tidal volume (mL)	223 ± 88*†	406 ± 121*	505 ± 143†	0.0012
Respiratory rate (bpm)	27 ± 6*†	19 ± 5*	17 ± 6†	0.0056
Sniff nasal inspiratory pressure (SNIP; cmH_2O)	11.9 ± 3.8†	18.9 ± 18.1*	50.7 ± 27.4*†	0.0009
Unassisted cough peak expiratory flow (L/min)	46 ± 43†	80.3 ± 51.0*	180 ± 83*†	0.0005
Parasternal electromyogram (EMGpara)	12.8 ± 7.8	6.6 ± 9.6	13.4 ± 6.1	ns
Neural respiratory drive (EMGpara%max)	53.9 ± 21.7*	42.7 ± 35.2	31.4 ± 17.7*	0.037
Oxygen saturation (SpO_2; %)	97.1 ± 2.0	97.3 ± 1.3	98.4 ± 2.1	ns
Transcutaneous CO_2 ($TcCO_2$; kPa)	6.3 ± 1.2	6.1 ± 1.5	5.8 ± 0.9	ns
Heart rate (bpm)	81 ± 17	73 ± 32	61 ± 27	ns
Borg score (0–10)	1.4 ± 1.3	1 ± 1.5	1 ± 1	ns

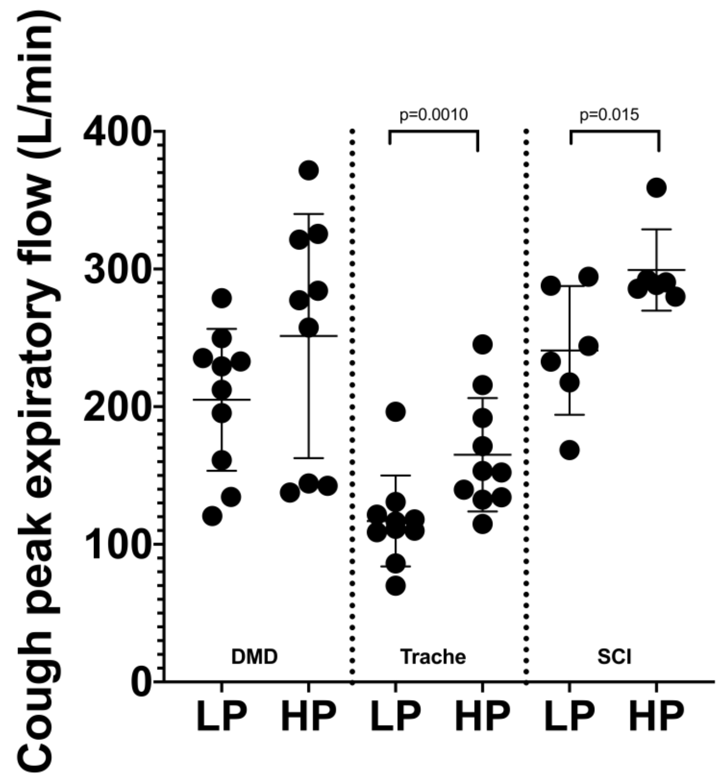
Results

		DMD (n=10)	LTTV (n=11)	SCI (n=8)	P-value
cPIF (L/min)	LP	130 ± 28	102 ± 22	135 ± 43	ns
	HP	155 ± 35*	116 ± 24*†	190 ± 46†	0.0011
	P-value	0.011	0.0011	0.0028	
cPEF (L/min)	LP	205 ± 52*	117 ± 33*†	241 ± 47†	<0.0001
	HP	251 ± 89*	165 ± 41*†	299 ± 30†	0.0008
	P-value	ns	0.0010	0.015	
cPEF-cPIF (L/min)	LP	75 ± 47*	15 ± 19*†	106 ± 77†	0.003
	HP	96 ± 65	49 ± 29	109 ± 62	ns
	P-value	ns	0.0057	ns	
cPEF:cPIF	LP	1.6 ± 0.4	1.2 ± 0.2*	2.0 ± 1.0*	0.011
	HP	1.6 ± 0.4	1.4 ± 0.3	1.7 ± 0.5	ns
	P-value	ns	0.013	ns	
Inspiratory volume (L)	LP	1.8 ± 1.0	2.2 ± 0.8	2.4 ± 1.3	ns
	HP	3.6 ± 1.9	3.1 ± 0.9	3.6 ± 1.3	ns
	P-value	0.025	0.0005	ns	
Expiratory	LP	1.7 ± 1.0	2.4 ± 0.7	2.6 ± 1.9	ns
	HP	2.4 ± 2.5	3.4 ± 0.7	3.8 ± 3.4	ns

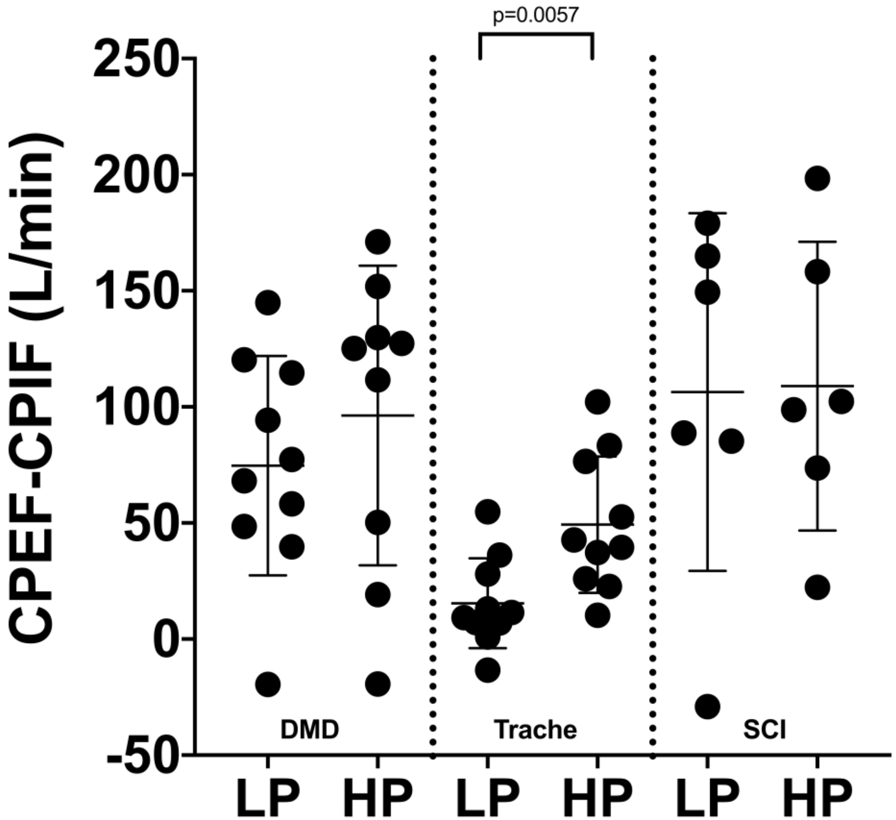
Results

cPIF and cPEF





Results



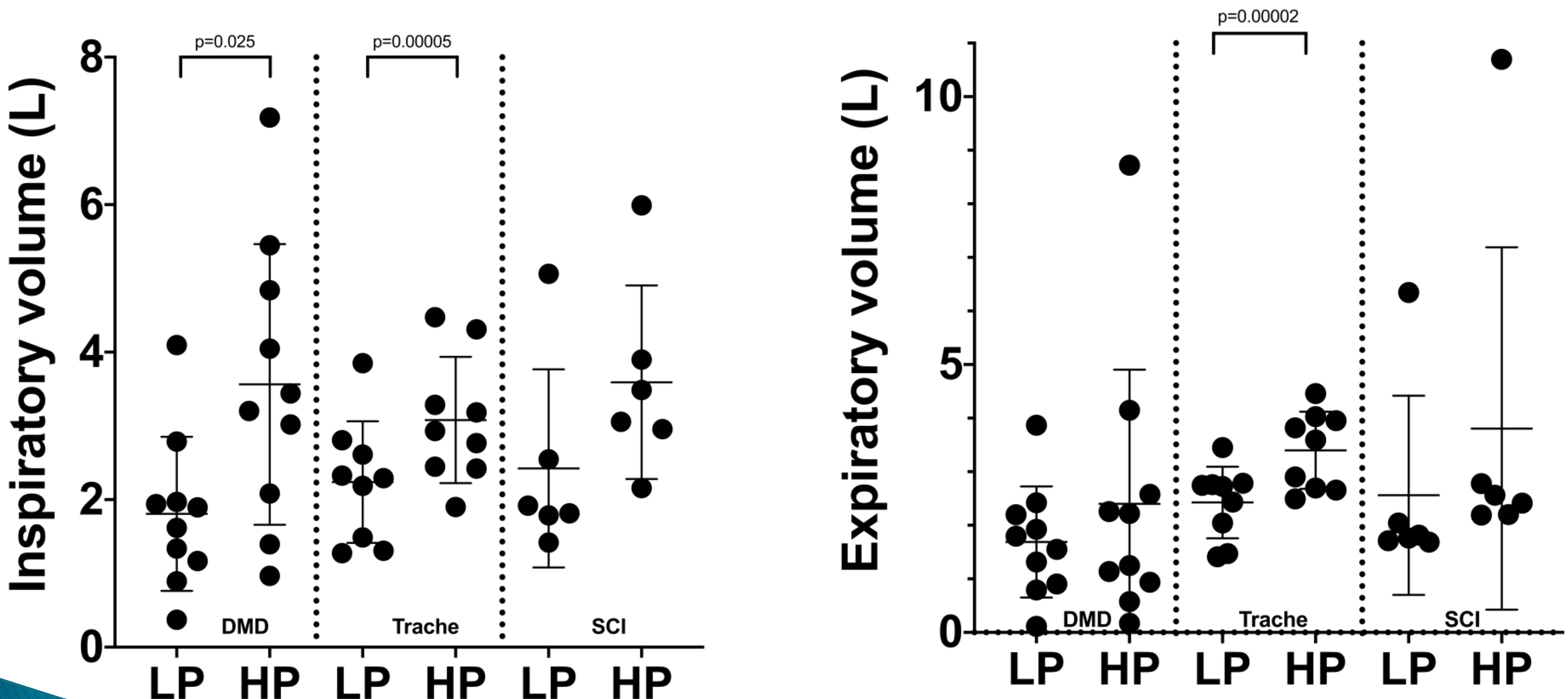
cPEF–cPIF

PEF-PIF >17L/min promotes mucous movement (Volpe et al. 2008)

	DMD (n=10)	Trache (n=11)	SCI (n=8)	P-value
LP	75 ± 47*	15 ± 19*†	106 ± 77†	0.003
HP	96 ± 65	49 ± 29	109 ± 62	ns
P-value	ns	0.0057	ns	

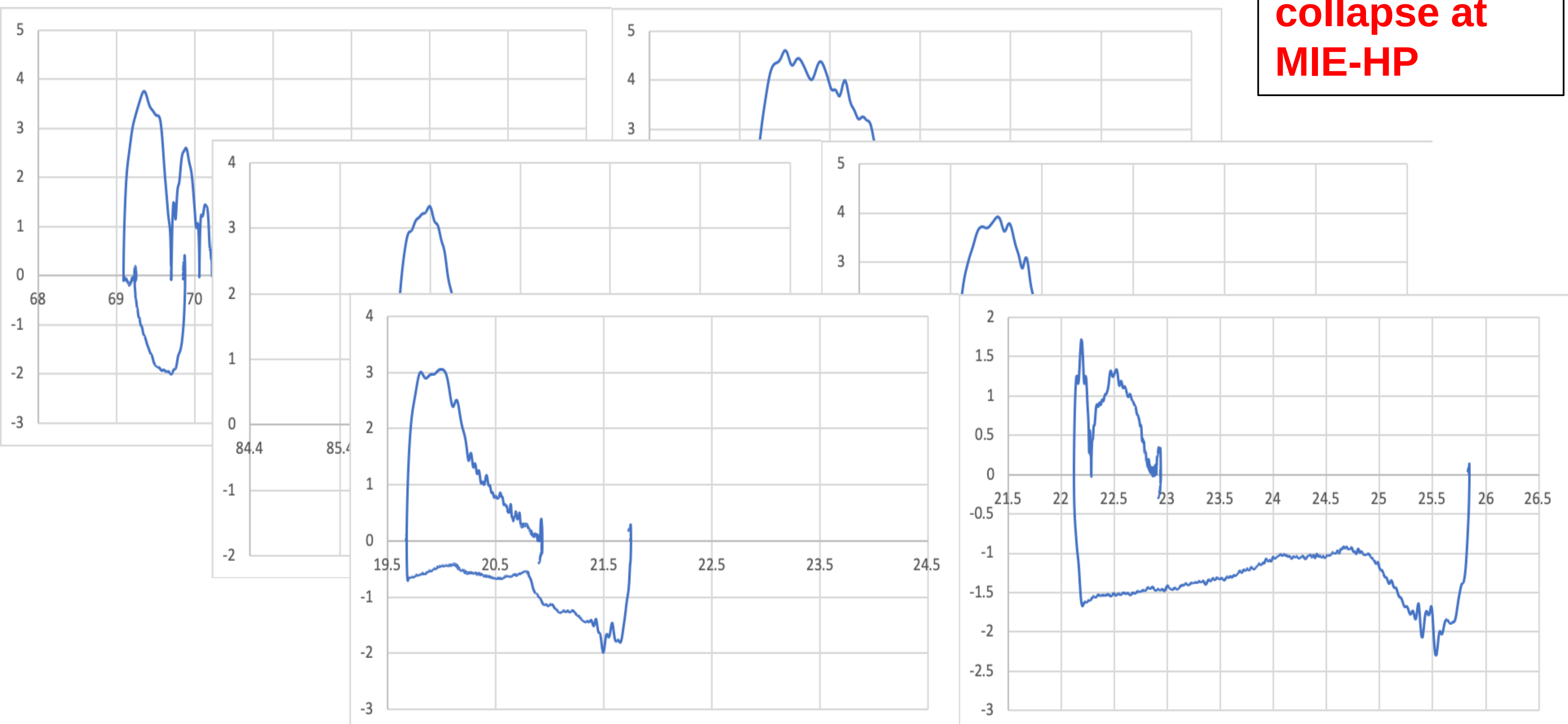
Results

Inspiratory and expiratory volume



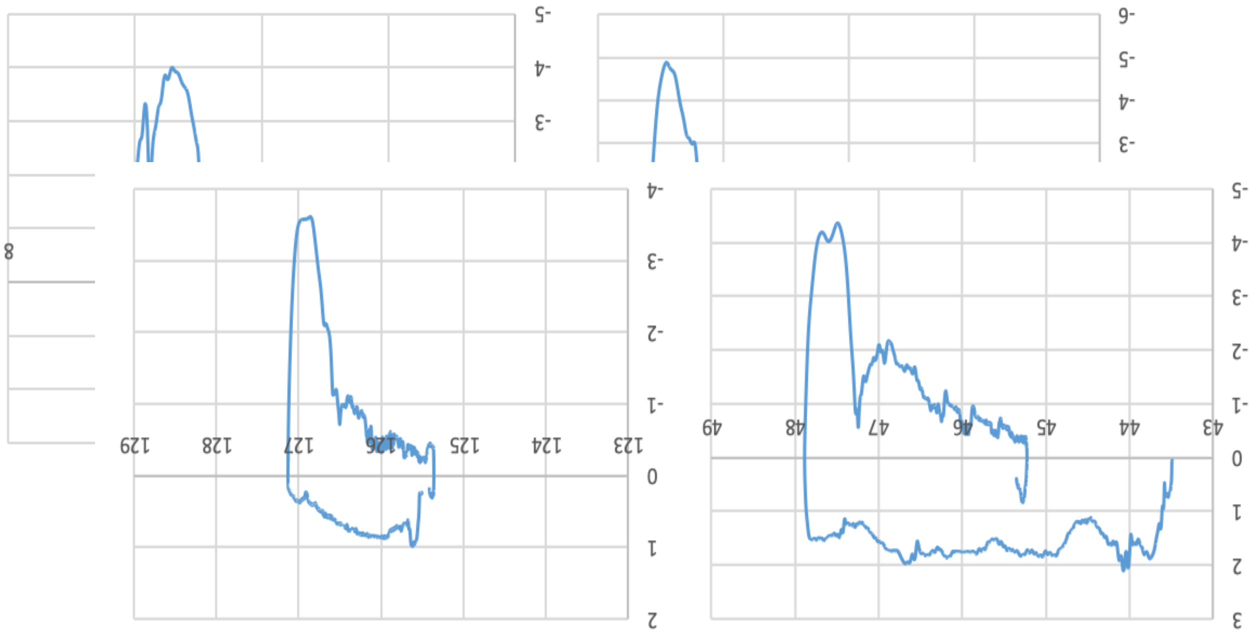
Duchenne Muscular Dystrophy

7/10 upper airway collapse at MIE-HP



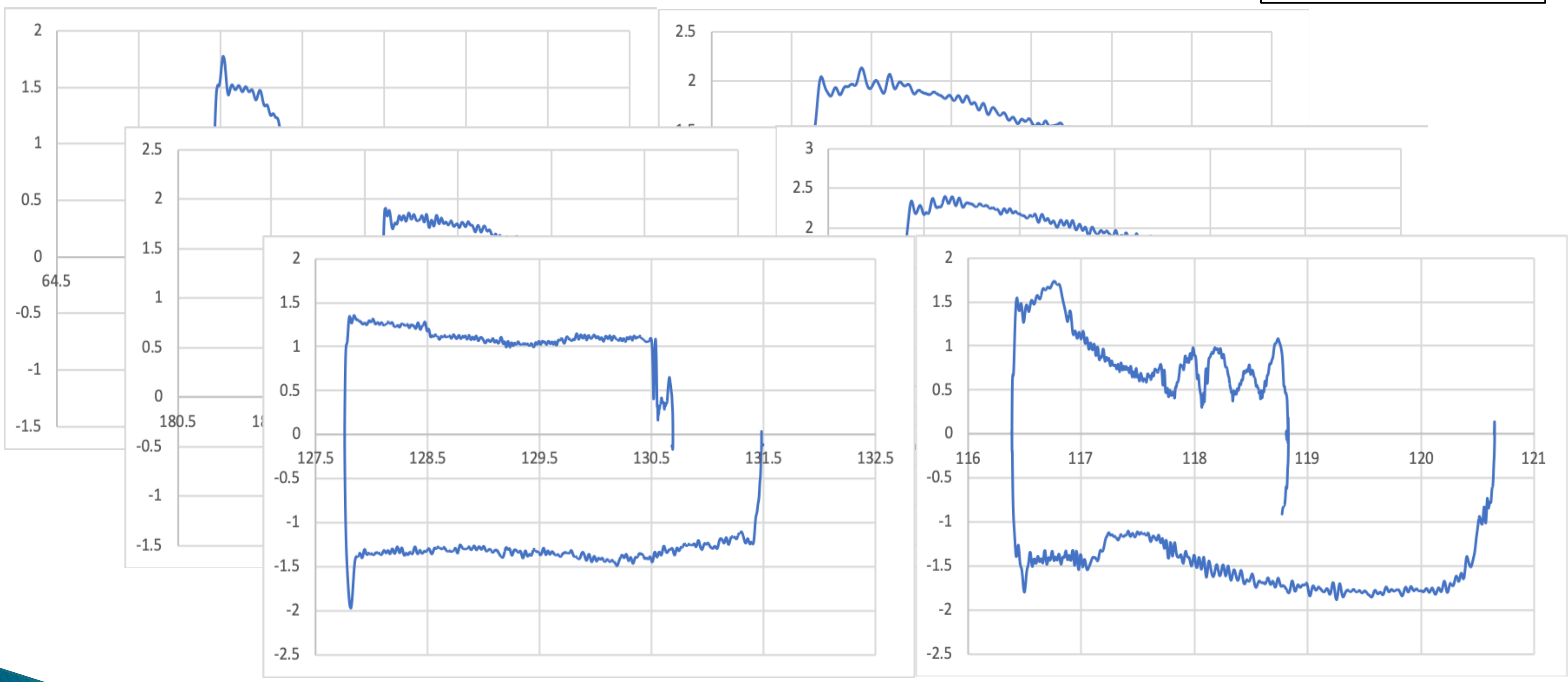
Spinal Cord Injury

1/6 upper airway collapse at MIE-HP



Tracheostomy

1/11 airway collapse at MIE-HP



Upper Airway Collapse

- **Bulbar dysfunction limits the increase in cPEF during MI-E** (Sancho 2004)
  - ?dynamic upper airway collapse

- **In ALS pts**, laryngeal adduction during insufflation and exsufflation at any pressure
  - More prominent in those with bulbar weakness (Andersen 2017)
- Healthy – laryngeal adduction of varying degrees (Andersen 2013)

- **Laryngoscopy** not readily available in clinical practice

- Using **flow-volume curves**, 15/27 NMD patients suffered upper airway collapse during MI-E (Lacombe 2019)

Conclusion

The three groups reflect different severity of respiratory muscle weakness and upper airway function

HP improves cPIF in all

cPEF doesn't improve in DMD

Both LP and HP create an **adequate flow bias**, **except LP in tracheostomy**

Frequent upper airway collapse observed in DMD

- ?cause of lack of improvement in cPEF

- **Data support use of HP-MIE in tracheostomy patients** and ?SCI?

- **HP-MIE is counterproductive** in patients with **bulbar involvement**

However

22 year old female

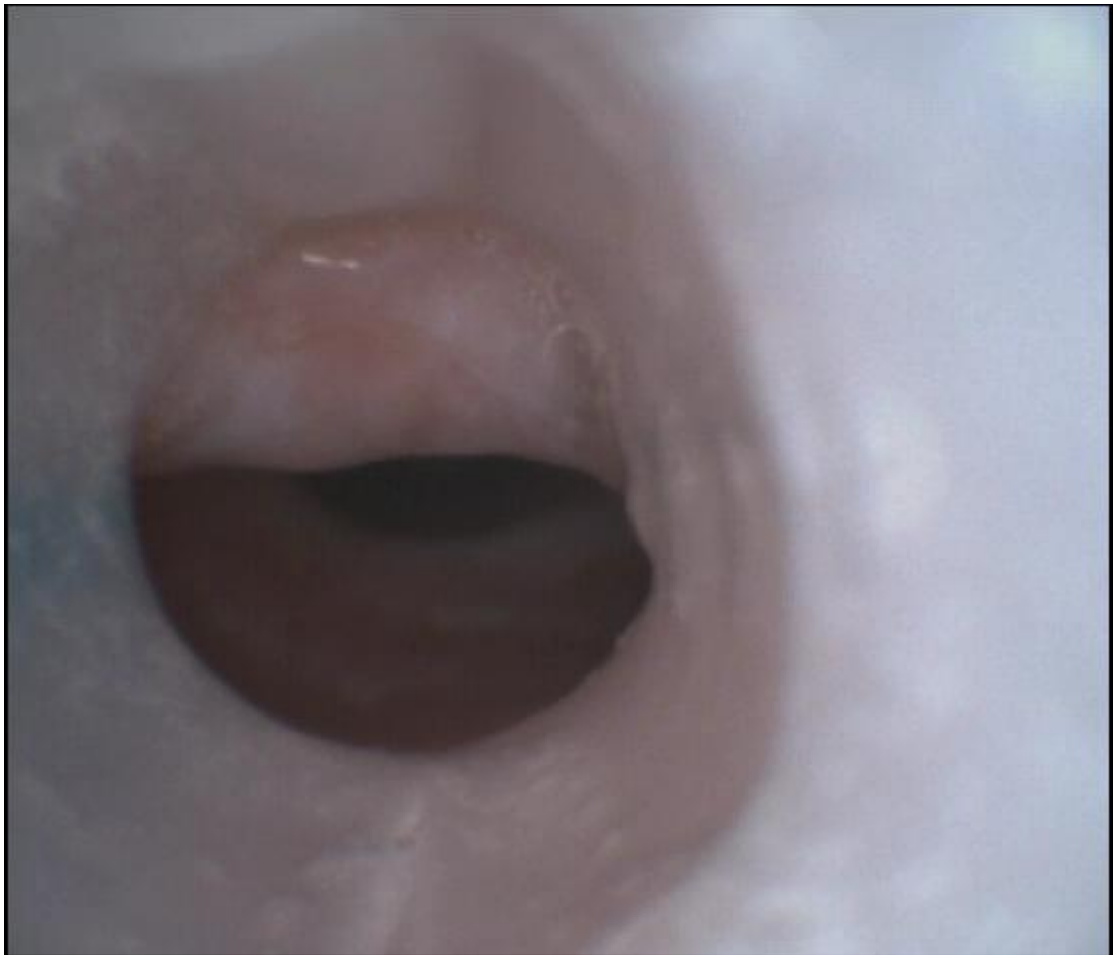
Pycnodysostosis Lysosomal Storage Disease

Invasively ventilated via a tracheostomy for 2 years

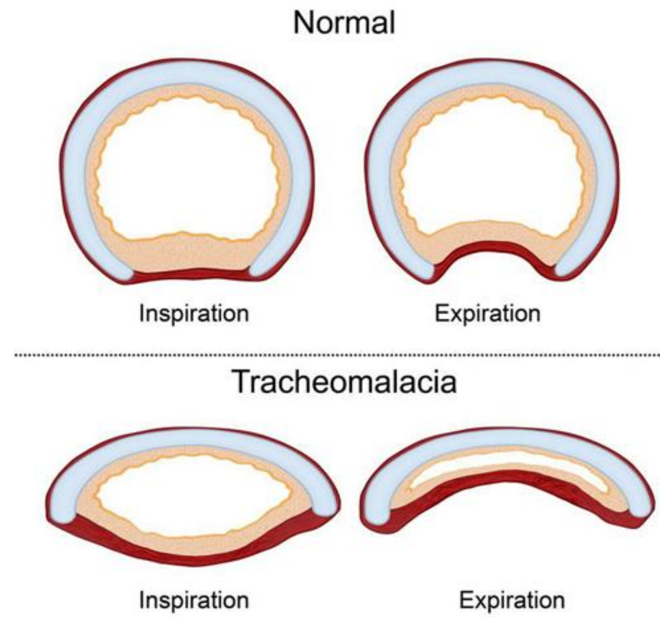
Established on MIE for secretions management

Debulking of recurrent granulation tissue occluding the lower end of the tracheostomy

Bronchoscopy under MIE



EDAC/TBM



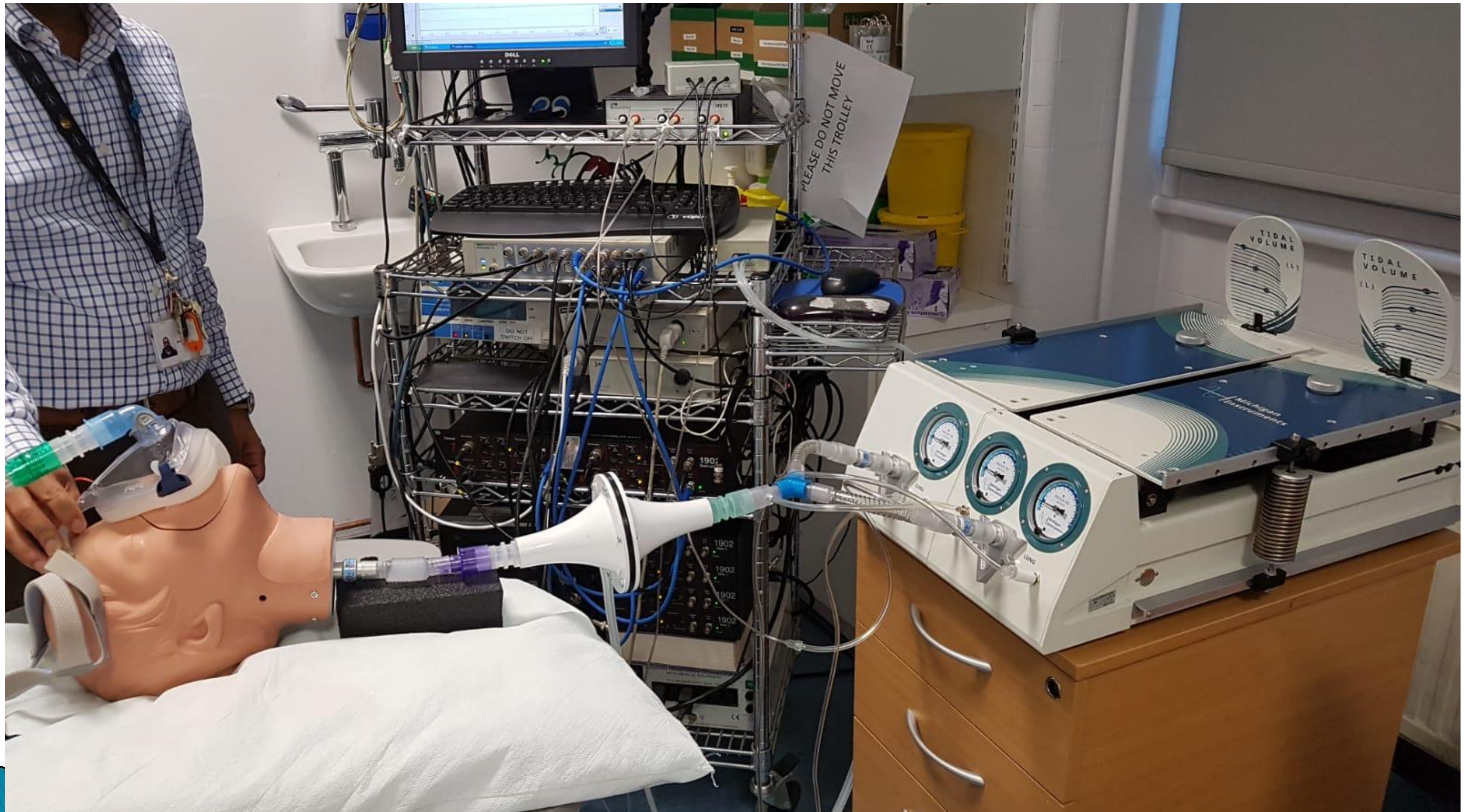
Abnormal weakening of the walls of the central airways leading to central airway collapse.

Treatment Options

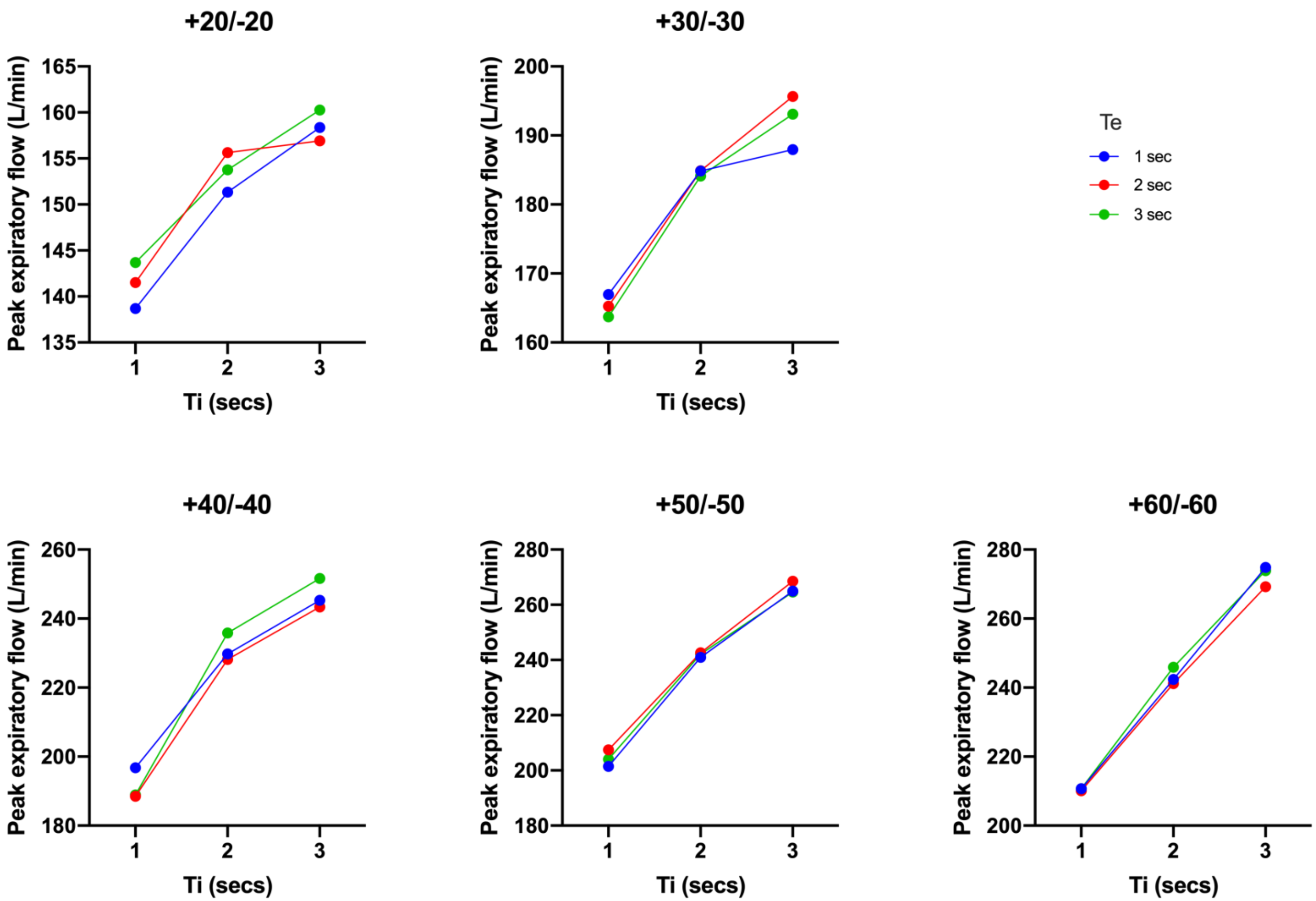
- Management of the underlying disease
- Endoscopic treatment (Airway stenting, Laser)
- Surgical tracheoplasty
- Nocturnal Non-Invasive Ventilation or CPAP

Carden KA et al. Chest 2005; 127:984.

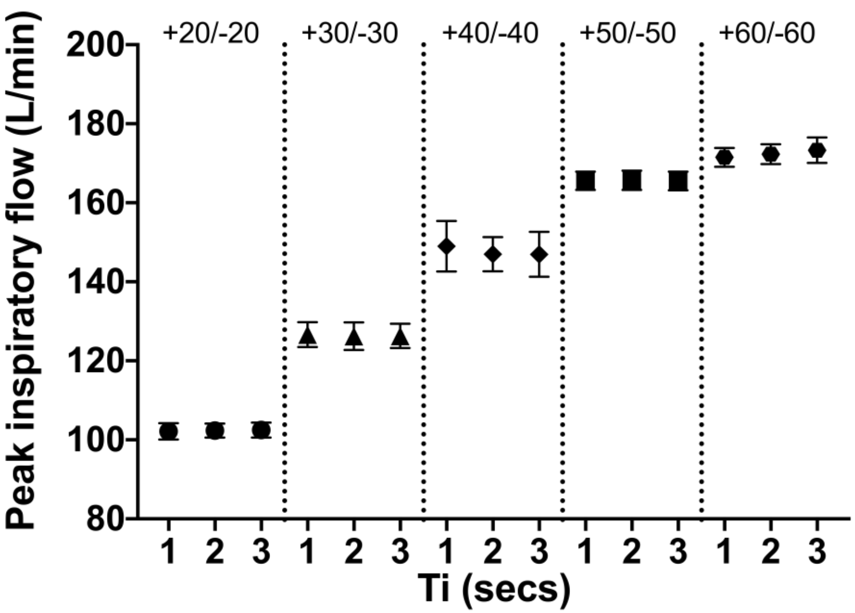
Artificial Lung Study

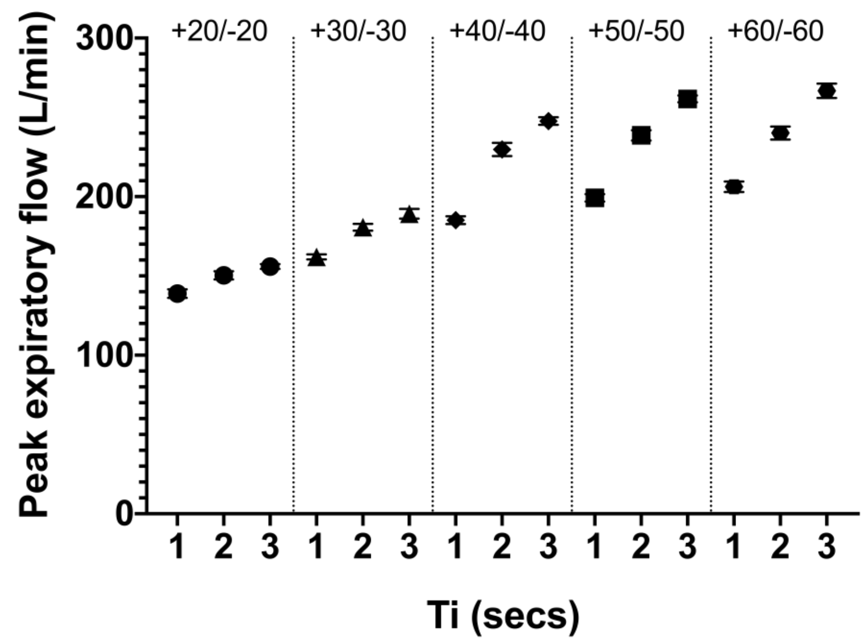


The effect of changing Ti / Te

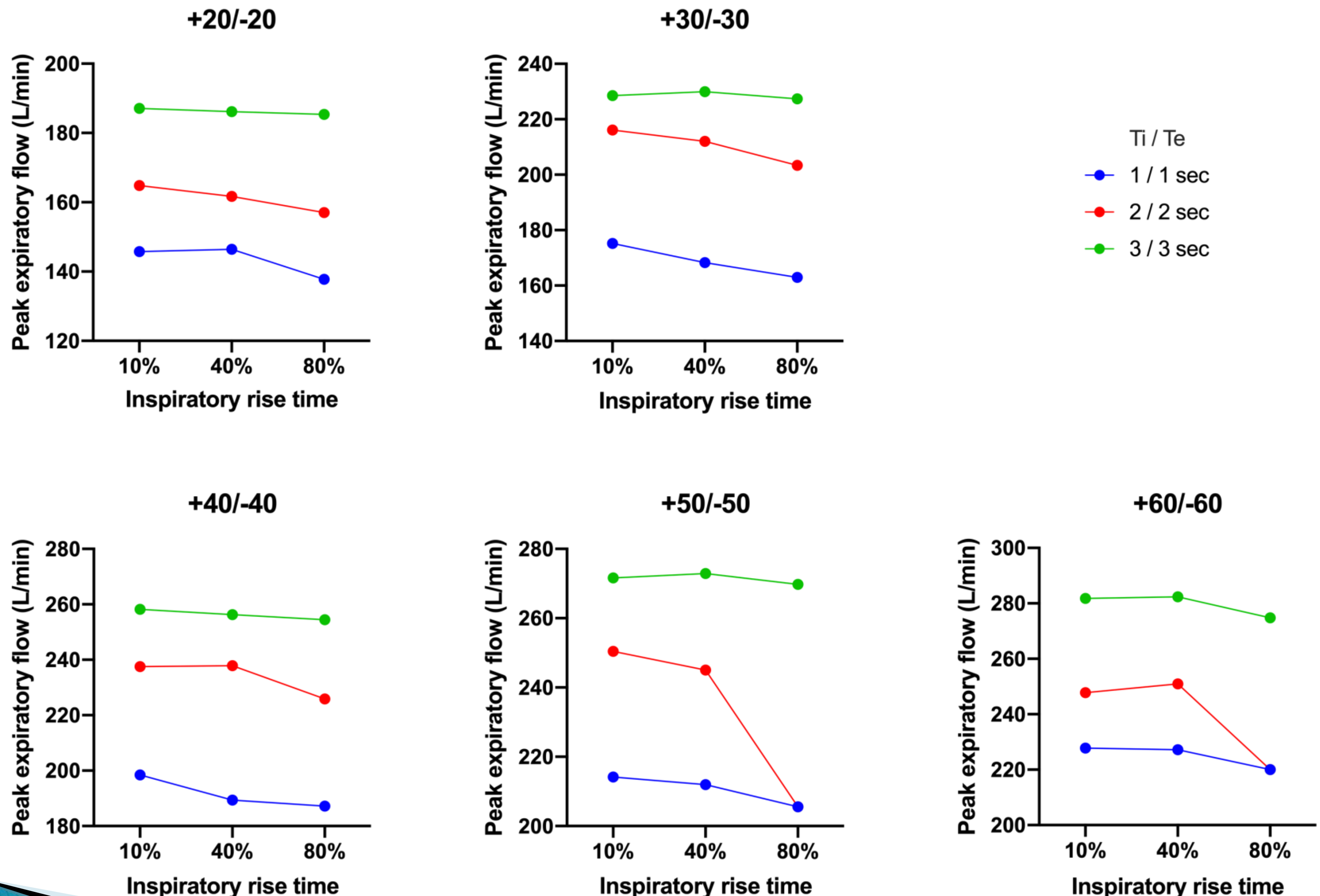


Increasing Ti at fixed Te of 3 seconds





Inspiratory Rise Time



Artificial Lung: Conclusion

- Increasing inspiratory time increases cPEF, regardless of pressure
- **Expiratory time doesn't impact on PEF**
- Up to +40/-40, PEF increases with pressure. Beyond this, T_i drives the PEF
- Increasing inspiratory rise time decreases cPEF

Thank You

Lane Fox Clinical Respiratory Physiology Research Centre, St Thomas's Hospital
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Prof Louise Rose, Ms Gill Arbane, Dr Patrick Murphy, Prof Nicholas Hart

Centre for Human and Applied Physiological Sciences, King's College London
Prof Steve Harridge, Dr Ged Rafferty, Dr Caroline Jolley

London Respiratory Muscle Group
Prof Michael Polkey, Prof Nicholas Hart, Dr Nicholas Hopkinson, Dr William Mann, Dr Patrick Murphy, Prof Joerg Steier,
Prof John Moxham

BREAS

Questions?

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Effectiveness

- Increase cough PEF by more than 80% (Bach 1993, Chatwin 2003)
- Reduce incidence of respiratory infection (Vianello 2005)
- Reduce time required for secretion clearance (Chatwin 2009)
- Patients prefer to suction (Boitano 2006)

ATS/ERS Statement on Respiratory Muscle Testing

This Joint Statement of the American Thoracic Society (ATS), and the European Respiratory Society (ERS) was adopted by the ATS Board of Directors, March 2001 and by the ERS Executive Committee, June 2001

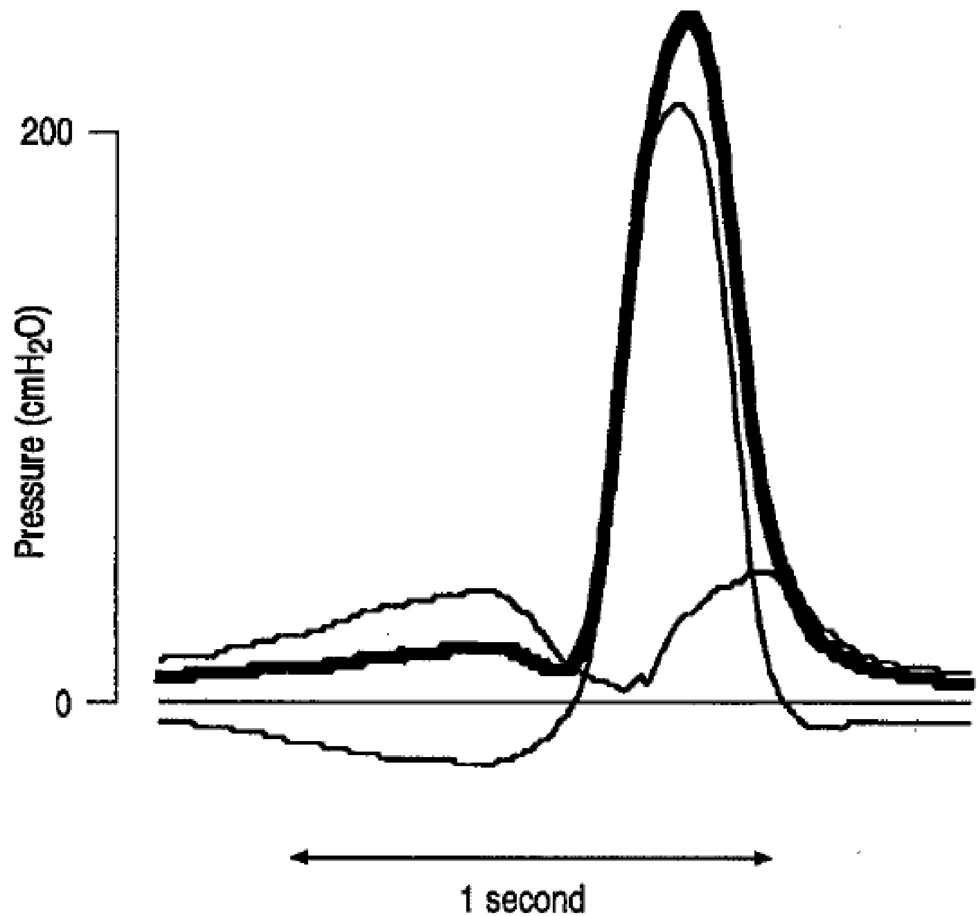

Figure 8. Pressures during a maximal voluntary cough in a normal subject showing high positive gastric pressures generated in abdomen (Pga; *thick line*) and esophagus (Pes) with low Pdi during the maneuver.