Case Study: Secondary Progressive MS

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Case Learning Objectives

- Identify need to examine respiratory muscle strength
- Identify need for respiratory muscle strength intervention
- Identify appropriate measurement tool for respiratory muscle assessment
- Identify appropriate respiratory muscle strength training protocol

Sue: Demographics

- 51 y.o. female
- Secondary progressive MS
- Onset 27 years prior
- EDSS = 2.5

Sue: Co-morbidities & Symptoms

Co-Morbidities

- Allergies
- Hepatitis A
- Arthritis
- Mild depression

Symptoms

- Fatigue
- Visual disturbance
- In-coordination
- Numbness/tingling
- Muscle weakness
- Dysphagia with gastric feeding tube

Sue: Medications & Activity Level

Medication

- Copaxone
- Baclofen
- Klonopin
- Neurontin
- Estrace

Activity Level

- Iyengar yoga 90 minutes twice/week
- Mild Hatha yoga 60 minutes once/week
- Out in community on a daily basis
- Works part-time

Sue: Need for Respiratory Muscle Examination

- Most people with MS do not complain about decreased respiratory function (Altintas, 2007)

- Maximal inspiratory pressure (MIP) and maximal expiratory pressure (MEP), indirect measures of pulmonary muscle strength, are both significantly reduced in patients with MS.

Altintas et al, Clin Neurol Neurosurg, 2007, 109(3):242-6

Sue: Need for Respiratory Muscle Examination

- In ambulatory patients with MS:
  - Average MIP values range from 55-77% of predicted values
  - Average MEP values range from 34-60% of predicted values
- In patients with MS who are primary wheelchair users or who are confined to the bed:
  - Average MIP values range from 27-74% of predicted values
  - Average MEP values range from 18-51% of predicted values

Buyse B, et al, Eur Resp J, 1997:10: 139-145. Chiara, et al 2006, Fry et al, 2007

Sue: Manometry Assessment Device

- Manometer to test:
  - Maximal Inspiratory Pressure (MIP)
  - Maximal Expiratory Pressure (MEP)

www.microdirect.com

Sue: Spirometry Assessment

- Spirometer to test (values obtainable dependent on device used):
  - Forced Vital Capacity (FVC)
  - Forced Expiratory Volume in 1 second (FEV1)
  - Peak Expiratory Flow (PEF)
  - Maximal Voluntary Ventilation (MVV)
- Values compared to normative data referencing gender, age, and height

Sue: Training Protocol

Protocol

- 10 weeks of daily exercise with a pressure threshold load trainer
- 3 sets of 15 repetitions
- Initial pressure set at 30% of MIP
- Weekly phone call to guide progression
- Progressed based on symptoms, RPE, and initial MIP

Respironic Inspiratory Muscle Trainer (IMT)

Adjustment of Training Threshold Load By Use of RPE

TABLE 1. Ten-Week Home IMT Exercise Training Protocol
Frequency: IMT exercises performed daily for 10 weeks.
Overload: Repetitions and Sets: Three sets of 15 repetitions*
Resistance: Initial resistance (H_2O cm) of the IMT was set at 30% of the subjects pretest MIP.
Progression: Subjects were called once per week by one of the investigators to assist with IMT pressure resistance training progression. IMT pressure resistance was progressed weekly according to the subject's baseline MIP pressure and RPE as well as the subject's symptoms

Subject's Baseline MIP Pressure: <50 cm H_2O				
Borg RPE	**<13**	**13 to 15**	**>15**	**>17**
Pressure resistance (cm H_2O)	Increased by 2	Increased by 1	Maintained at same level	Reduced by 2
Subject's Baseline MIP pressure: >50 cm H_2O				
Borg RPE	**<13**	**13 to 15**	**>15**	**>17**
Pressure resistance (cm H_2O)	Increased by 4	Increased by 2	Maintained at same level	Reduced by 2

If subjects developed symptoms (ie, dizziness, lightheadedness, or shortness of breath) while performing IMT exercises, the resistance was adjusted as follows until no symptoms persisted.

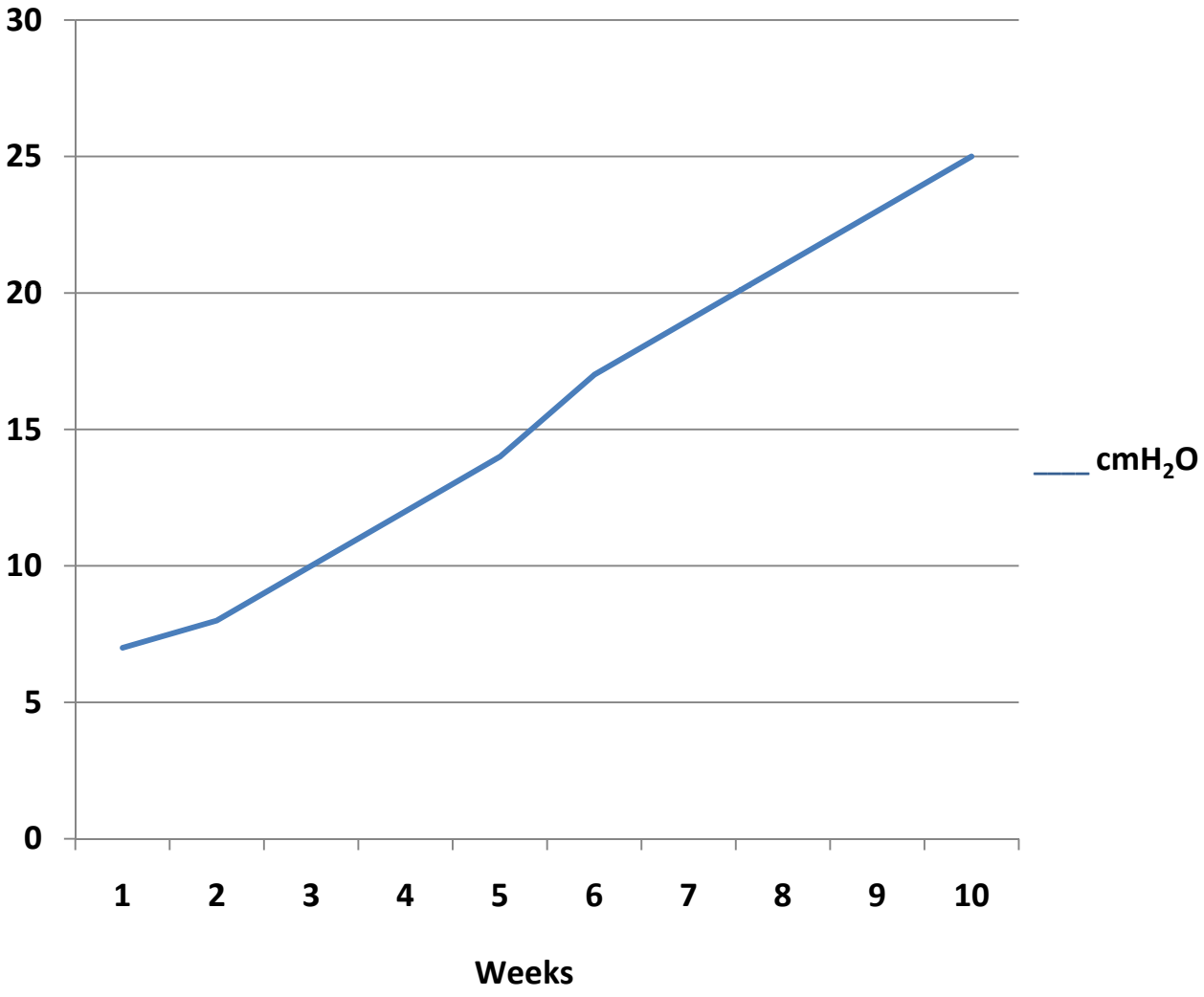
Symptoms	Two or more symptomatic episodes in a row per week	1–2 isolated symptomatic episodes per week
Pressure resistance (cm H_2O)	Decreased by 2 subjects were called back 3 days later to monitor subject's response	Held constant, subjects were called back 3 days later to monitor subject's response

* If a subject achieved the maximum IMT Trainer pressure resistance of 41 cm H_2O and resistance could no longer be increased, a fourth set of exercises was added along with an increased number of repetitions up to a maximum of 15 repetitions.

Abbreviations: IMT, inspiratory muscle strength training; MIP, maximal inspiratory pressure; RPE, rating of perceived exertion.

Fry et al, 2007

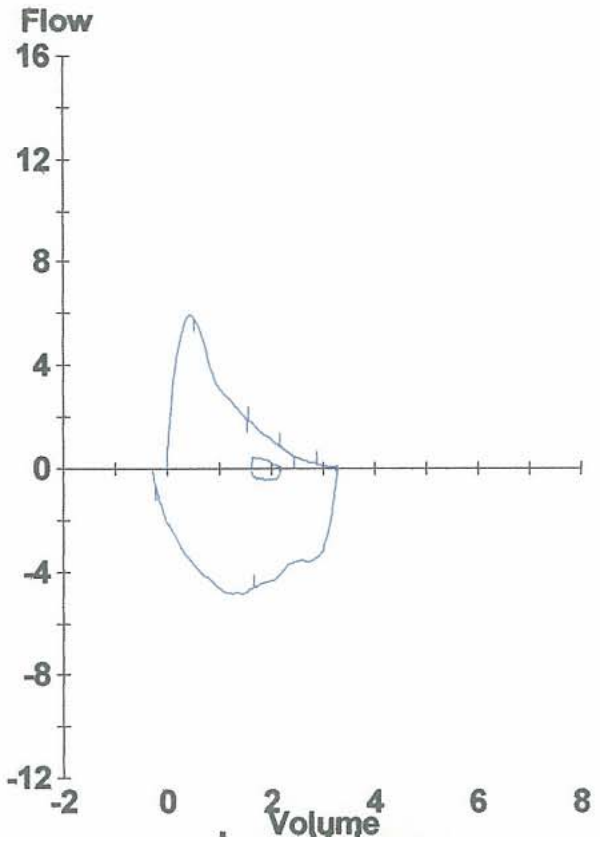
Sue: IMT Exercise Progression



Sue: Demographics

- 51 y.o. female
- Secondary progressive MS
- Onset 27 years prior
- EDSS = 2.5

Sue: Spirometry



Gender: Female Age: 51
Diagnosis: Secondary Progressive

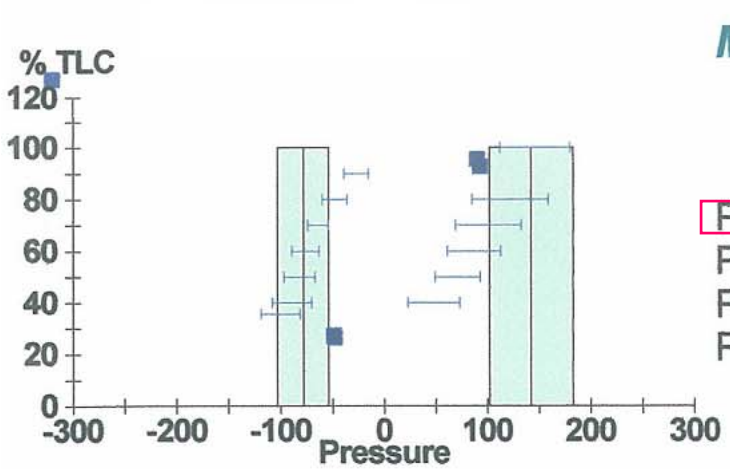
Spirometry

		Ref	Pre Meas	Pre % Ref	Post Meas	Post % Ref	Post % Chg
FVC	Liters	3.28	3.29	100	3.78	115	15
FEV1	Liters	2.49	2.20	88	2.41	97	9
FEV1/FVC	%	75	67		64		
FEF25-75%	L/sec	2.86	1.27	44	1.26	44	-1
PEF	L/sec	5.95	5.93	100	6.57	110	11
FET100%	Sec		9.30		11.48		23
FIVC	Liters	3.28	3.55	108	3.45	105	-3
FIF50%	L/sec		4.60		5.54		20
FVL ECode			000000		000000		
MVV	L/min	99	89	90	111	112	25
MVV 6	L/min		85		109		28
f	BPM		65		110		69

Sue: Discussion of Spirometry Results

- Sue was in relatively normal range for spirometry measures.
- Improved function in primary values of interest:
  - FVC
  - FEV1
  - PEF
  - MVV

Sue: Manometry



Maximal Respiratory Pressures

		Ref	Pre Meas	Pre % Ref	Post Meas	Post % Ref	Post % Chg
PI max	cmH2O	78	49	63	83	106	69
PI Volume	Liters		0.95		1.14		20
PE max	cmH2O	143	93	65	107	75	15
PE Volume	Liters		2.05		2.27		11

Sue: Discussion of Manometry Results

- Baseline values at 63% for MIP and 65% for MEP.
  - Any value under 60% of predicted for MIP and MEP is considered clinically abnormal.
- Increase of 69% in MIP and 15% in MEP following IMT strengthening.

Sue: Discussion of Spirometry and Manometry Results

- Respiratory muscle weakness must be approximately less than 50% of normal to see reduction in spirometry values. (Rochester, 1994)
- Sue displayed significant respiratory muscle weakness even with relatively normal spirometry values.
- Thus, manometry is a more sensitive measure of respiratory muscle dysfunction in persons with MS.

Rochester DF, Esau SA. Clin Chest Med 1994. 15(4):751-63

Sue: Functional Outcomes

Activity	Pre-test	Post-test
Single Limb Stance	4.38 seconds	14.53 seconds
Functional Stair Test	3.78 seconds	3.13 seconds
Sit-to-Stand Test	10.75 seconds	9.60 seconds
Six Minute Walk Test	1712 feet	1807 feet
Fatigue Severity Scale (7 point likert scale)	Mean score = 6	Mean score = 3.3

Sue: Anecdotal Follow-up

- Sue continued to use the IMT for one year following the study because she felt it was helpful.
- Continues with Iyengar yoga with strong emphasis on breathing

References on Respiratory Muscle

- ATS/ERS Statement on respiratory muscle testing. *Am J Respir Crit Care Med.* Aug 15 2002;166(4):518-624.
- Aiello M, Rampello A, Granella F, et al. Cough efficacy is related to the disability status in patients with multiple sclerosis. *Respiration.* 2008;76(3):311-316.
- Aisen M, Arlt G, Foster S. Diaphragmatic paralysis without bulbar or limb paralysis in multiple sclerosis. *Chest.* Aug 1990;98(2):499-501.
- Altintas A, Demir T, Ikitimur HD, Yildirim N. Pulmonary function in multiple sclerosis without any respiratory complaints. *Clin Neurol Neurosurg.* Apr 2007;109(3):242-246.
- Auer RN, Rowlands CG, Perry SF, Remmers JE. Multiple sclerosis with medullary plaques and fatal sleep apnea (Ondine's curse). *Clin Neuropathol.* Mar-Apr 1996;15(2):101-105.
- Balbierz JM, Ellenberg M, Honet JC. Complete hemidiaphragmatic paralysis in a patient with multiple sclerosis. *Am J Phys Med Rehabil.* Aug 1988;67(4):161-165.
- Berlin L, Kurtzke JF, Guthrie TC. Acute respiratory failure in multiple sclerosis and its management. *Trans Am Neurol Assoc.* 1952;56(77th Meeting):234-235.
- Beukelman DR, Kraft GH, Freal J. Expressive communication disorders in persons with multiple sclerosis: a survey. *Arch Phys Med Rehabil.* Oct 1985;66(10):675-677.

References on Respiratory Muscle

- Boor JW, Johnson RJ, Canales L, Dunn DP. Reversible paralysis of automatic respiration in multiple sclerosis. *Arch Neurol.* Nov 1977;34(11):686-689.
- Brown MG, Kirby S, Skedgel C, et al. How effective are disease-modifying drugs in delaying progression in relapsing-onset MS? *Neurology.* Oct 9 2007;69(15):1498-1507.
- Brown MG, Murray TJ, Sketris IS, et al. Cost-effectiveness of interferon beta-1b in slowing multiple sclerosis disability progression. First estimates. *Int J Technol Assess Health Care.* Summer 2000;16(3):751-767.
- Brück W. Inflammatory demyelination is not central to the pathogenesis of multiple sclerosis. *Journal of Neurology* 2005;252(Supplement 5):v10 - v15
- Buyse B, Demedts M, Meekers J, Vandegaer L, Rochette F, Kerkhofs L. Respiratory dysfunction in multiple sclerosis: a prospective analysis of 60 patients. *Eur Respir J.* Jan 1997;10(1):139-145.
- Carter JL, Noseworthy JH. Ventilatory dysfunction in multiple sclerosis. *Clin Chest Med.* Dec 1994;15(4):693-703.
- Chang A, Tourtellotte WW, Rudick R, Trapp BD. Premyelinating oligodendrocytes in chronic lesions of multiple sclerosis. *N Engl J Med.* Jan 17 2002;346(3):165-173.

References on Respiratory Muscle

- Chetta A, Rampello A, Marangio E, et al. Cardiorespiratory response to walk in multiple sclerosis patients. *Respir Med.* Jun 2004;98(6):522-529.
- Chiara T. *Expiratory muscle strength training in individuals with multiple sclerosis and healthy controls* [Dissertaion]. Gainesville FL: Physical Therapy, University of Florida, Gainesville, FL; 2003.
- Chiara T, Martin AD, Davenport PW, Bolser DC. Expiratory muscle strength training in persons with multiple sclerosis having mild to moderate disability: effect on maximal expiratory pressure, pulmonary function, and maximal voluntary cough. *Arch Phys Med Rehabil.* Apr 2006;87(4):468-473.
- Chiara T, Martin D, Sapienza C. Expiratory muscle strength training: speech production outcomes in patients with multiple sclerosis. *Neurorehabil Neural Repair.* May-Jun 2007;21(3):239-249.
- Compston A. The story of Multiple Sclerosis. *McAlpine's Multiple Sclerosis*. 4th ed: Churchill Livingstone.
- Cooper CB, Trend PS, Wiles CM. Severe diaphragm weakness in multiple sclerosis. *Thorax.* Aug 1985;40(8):633-634.

References on Respiratory Muscle

- Darley FL, Brown JR, Goldstein NP. Dysarthria in multiple sclerosis. *J Speech Hear Res.* Jun 1972;15(2):229-245.
- Espir M, Millac P. Paroxysmal brain stem dysfunction in multiple sclerosis. *Br Med J.* Dec 18 1976;2(6050):1503.
- Espir ML, Watkins SM, Smith HV. Paroxysmal dysarthria and other transient neurological disturbances in disseminated sclerosis. *J Neurol Neurosurg Psychiatry.* Aug 1966;29(4):323-330.
- Filippi M, Rocca MA. MRI evidence for multiple sclerosis as a diffuse disease of the central nervous system. *J Neurol.* Oct 2005;252 Suppl 5:v16-v24.
- Fry DK, Pfalzer LA, Chokshi AR, Wagner MT, Jackson ES. Randomized control trial of effects of a 10-week inspiratory muscle training program on measures of pulmonary function in persons with multiple sclerosis. *J Neurol Phys Ther.* Dec 2007;31(4):162-172.
- Fukuda H, Kitani M. [Acute respiratory arrest associated with medullary lesion in a case of multiple sclerosis]. *Rinsho Shinkeigaku.* Jul 1993;33(7):787-790.
- Gentiloni N, Schiavino D, Della Corte F, Ricci E, Colosimo C. Neurogenic pulmonary edema: a presenting symptom in multiple sclerosis. *Ital J Neurol Sci.* Jun 1992;13(5):435-438.

References on Respiratory Muscle

- Giroud M, Guard O, Dumas R. [Cardio-respiratory anomalies in disseminated sclerosis]. *Rev Neurol (Paris).* 1988;144(4):284-288.
- Gosselink R, Kovacs L, Decramer M. Respiratory muscle involvement in multiple sclerosis. *Eur Respir J.* Feb 1999;13(2):449-454.
- Gosselink R, Kovacs L, Ketelaer P, Carton H, Decramer M. Respiratory muscle weakness and respiratory muscle training in severely disabled multiple sclerosis patients. *Arch Phys Med Rehabil.* Jun 2000;81(6):747-751.
- Grasso MG, Lubich S, Guidi L, Rinnenburger D, Paolucci S. Cerebellar deficit and respiratory impairment: a strong association in multiple sclerosis? *Acta Neurol Scand.* Feb 2000;101(2):98-103.
- Guthrie TC, Kurtzke JF, Berlin L. Acute respiratory failure in multiple sclerosis and its management. *Ann Intern Med.* Dec 1952;37(6):1197-1203.
- Harrer G, Harrer H, Mayr A. [Autonomic dysfunction in multiple sclerosis (respiratory and cardiac disturbances) (author's transl)]. *Wien Klin Wochenschr.* Sep 12 1980;92(17):613-616.
- Hartelius L, Buder EH, Strand EA. Long-term phonatory instability in individuals with multiple sclerosis. *J Speech Lang Hear Res.* Oct 1997;40(5):1056-1072.

References on Respiratory Muscle

- Hartelius L, Nord L, Buder EH. Acoustic analysis of dysarthria associated with multiple sclerosis. *Clinical Linguistics & Phonetics.* 1995;9(2):95-120.
- Hartelius L, Runmarker B, Andersen O. Prevalence and characteristics of dysarthria in a multiple-sclerosis incidence cohort: relation to neurological data. *Folia Phoniatr Logop.* Jul-Aug 2000;52(4):160-177.
- Hartelius L, Runmarker B, Andersen O, Nord L. Temporal speech characteristics of individuals with multiple sclerosis and ataxic dysarthria: 'scanning speech' revisited. *Folia Phoniatr Logop.* Sep-Oct 2000;52(5):228-238.
- Howard RS, Wiles CM, Hirsch NP, Loh L, Spencer GT, Newsom-Davis J. Respiratory involvement in multiple sclerosis. *Brain.* Apr 1992;115 (Pt 2):479-494.
- Klefbeck B, Hamrah Nedjad J. Effect of inspiratory muscle training in patients with multiple sclerosis. *Arch Phys Med Rehabil.* Jul 2003;84(7):994-999.
- Koseoglu BF, Gokkaya NK, Ergun U, Inan L, Yesiltepe E. Cardiopulmonary and metabolic functions, aerobic capacity, fatigue and quality of life in patients with multiple sclerosis. *Acta Neurol Scand.* Oct 2006;114(4):261-267.
- Kurtzke JF. Rating neurologic impairment in multiple sclerosis: an expanded disability status scale (EDSS). *Neurology.* Nov 1983;33(11):1444-1452.

References on Respiratory Muscle

- Kuwahira I, Kondo T, Ohta Y, Yamabayashi H. Acute respiratory failure in multiple sclerosis. *Chest.* Jan 1990;97(1):246-248.
- Lagueny A, Arnaud A, Le Masson G, Burbaud P, Deliac P, Marthan R. Study of Central and peripheral conductions to the diaphragm in 22 patients with definite multiple sclerosis. *Electromyogr Clin Neurophysiol.* Sep 1998;38(6):333-342.
- Lamotte D, Thoumie P. [Multiple sclerosis and botulinum toxin]. *Ann Readapt Med Phys.* Jul 2003;46(6):299-302.
- Melin J, Usenius JP, Fogelholm R. Left ventricular failure and pulmonary edema in acute multiple sclerosis. *Acta Neurol Scand.* May 1996;93(5):315-317.
- Miscio G, Guastamacchia G, Priano L, Baudo S, Mauro A. Are the neurophysiological techniques useful for the diagnosis of diaphragmatic impairment in multiple sclerosis (MS)? *Clin Neurophysiol.* Jan 2003;114(1):147-153.
- Mochizuki A, Yamanouchi H, Murata M, Nagura H, Kuzuhara S, Toyokura Y. Medullary lesion revealed by MRI in a case of MS with respiratory arrest. *Neuroradiology.* 1988;30(6):574-576.
- Murdoch BE, Theodoros DG, eds. *Speech and Language Disorders, Multiple Sclerosis.* 1st ed. London and Philadelphia: Whurr Publishers Ltd; 2000.

References on Respiratory Muscle

- Murray J. Prelude to the framing of a disease: multiple sclerosis in the period before Charcots Lecons. *Int MS J.* Dec 2004;11(3):79-85.
- Murray J. *Multiple Sclerosis:The history of the disease*. 1st ed. New York, NY, USA: Demos Medical Publishing; 2005.
- Mutluay FK, Demir R, Ozyilmaz S, Caglar AT, Altintas A, Gurses HN. Breathing-enhanced upper extremity exercises for patients with multiple sclerosis. *Clin Rehabil.* Jul 2007;21(7):595-602.
- Mutluay FK, Gurses HN, Saip S. Effects of multiple sclerosis on respiratory functions. *Clin Rehabil.* Jun 2005;19(4):426-432.
- Olgiati R, Girr A, Hugi L, Haegi V. Respiratory muscle training in multiple sclerosis: a pilot study. *Schweiz Arch Neurol Psychiatr.* 1989;140(1):46-50.
- Olgiati R, Jacquet J, Di Prampero PE. Energy cost of walking and exertional dyspnea in multiple sclerosis. *Am Rev Respir Dis.* Nov 1986;134(5):1005-1010.
- Pappalardo A, Patti F, Restivo DA, Reggio A. [Symptomatic management in multiple sclerosis]. *Clin Ter.* Nov-Dec 2004;155(11-12):505-528.
- Pearce JMS. Historical Descriptions of Multiple Sclerosis: The stories of Augustus D'Este and *The Journal of a Disappointed Man*. *European Neurology.* May 3, 2005 2005;54:49-53.

References on Respiratory Muscle

- Pinedo A, Mateo I, Garcia-Monco JC. [Multiple sclerosis and acute weakness of the bulbar and respiratory muscles]. *Neurologia.* May 2004;19(4):213-214.
- Pittock SJ, Rodriguez M, Wijdicks EF. Rapid weaning from mechanical ventilator in acute cervical cord multiple sclerosis lesion after steroids. *Anesth Analg.* Dec 2001;93(6):1550-1551, table of contents.
- Popova LM, Avdiunina IA, Alferova VP. [Respiratory failure in disseminated sclerosis]. *Anesteziol Reanimatol.* Jul-Aug 2000(4):59-63.
- Poser CM, Brinar VV. Diagnostic criteria for multiple sclerosis. *Clin Neurol Neurosurg.* Apr 2001;103(1):1-11.
- Poser CM, Brinar VV. The accuracy of prevalence rates of multiple sclerosis: a critical review. *Neuroepidemiology.* 2007;29(3-4):150-155.
- Poser CM, Paty DW, Scheinberg L, et al. New diagnostic criteria for multiple sclerosis: guidelines for research protocols. *Ann Neurol.* Mar 1983;13(3):227-231.
- Rae-Grant AD, Eckert NJ, Bartz S, Reed JF. Sensory symptoms of multiple sclerosis: a hidden reservoir of morbidity. *Mult Scler.* Jun 1999;5(3):179-183.

References on Respiratory Muscle

- Rasova K, Brandejsky P, Havrdova E, Zalisova M, Rexova P. Spiroergometric and spirometric parameters in patients with multiple sclerosis: are there any links between these parameters and fatigue, depression, neurological impairment, disability, handicap and quality of life in multiple sclerosis? *Mult Scler.* Apr 2005;11(2):213-221.
- Rasova K, Havrdova E, Brandejsky P, Zalisova M, Foubikova B, Martinkova P. Comparison of the influence of different rehabilitation programmes on clinical, spirometric and spiroergometric parameters in patients with multiple sclerosis. *Mult Scler.* Apr 2006;12(2):227-234.
- Rizvi SS, Ishikawa S, Faling LJ, Schlessinger L, Satia J, Seckel B. Defect in automatic respiration in a case of multiple sclerosis. *Am J Med.* Apr 1974;56(4):433-436.
- Rontal E, Rontal M, Wald J, Rontal D. Botulinum toxin injection in the treatment of vocal fold paralysis associated with multiple sclerosis: a case report. *J Voice.* Jun 1999;13(2):274-279.
- Rovaris M, Gambini A, Gallo A, et al. Axonal injury in early multiple sclerosis is irreversible and independent of the short-term disease evolution. *Neurology.* Nov 22 2005;65(10):1626-1630.

References on Respiratory Muscle

- Sapir S, Pawlas A, Ramig L, Seeley E, Fox C, Corboy J. Effect of intensive phonatory-respiratory treatment (LSVT) on voice in two individuals with multiple sclerosis. *J Medical Speech-Language Pathology* 2001;9(2):141-151.
- Savci S, Inal-Ince D, Arikan H, et al. Six-minute walk distance as a measure of functional exercise capacity in multiple sclerosis. *Disabil Rehabil.* Nov 30 2005;27(22):1365-1371.
- Smeltzer S. An index for clinical assessment of pulmonary dysfunction in multiple sclerosis. *N J Nurse.* Jul-Aug 1990;20(4):16, 15.
- Smeltzer SC, Lavietes MH. Reliability of maximal respiratory pressures in multiple sclerosis. *Chest.* Jun 1999;115(6):1546-1552.
- Smeltzer SC, Lavietes MH, Cook SD. Expiratory training in multiple sclerosis. *Arch Phys Med Rehabil.* Sep 1996;77(9):909-912.
- Smeltzer SC, Lavietes MH, Troiano R, Cook SD. Testing of an Index of Pulmonary Dysfunction in Multiple Sclerosis. *Nurs Res.* Nov-Dec 1989;38(6):370-374.
- Smeltzer SC, Skurnick JH, Troiano R, Cook SD, Duran W, Lavietes MH. Respiratory function in multiple sclerosis. Utility of clinical assessment of respiratory muscle function. *Chest.* Feb 1992;101(2):479-484.

References on Respiratory Muscle

- Smeltzer SC, Utell MJ, Rudick RA, Herndon RM. Pulmonary function and dysfunction in multiple sclerosis. *Arch Neurol.* Nov 1988;45(11):1245-1249.
- Smith PF. Cannabinoids in the treatment of pain and spasticity in multiple sclerosis. *Curr Opin Investig Drugs.* Jun 2002;3(6):859-864.
- Summerfield R, Tubridy N, Sirker A, Banner NR, Peatfield RC. Pulmonary oedema with multiple sclerosis. *J R Soc Med.* Aug 2002;95(8):401-402.
- Tantucci C, Massucci M, Piperno R, Betti L, Grassi V, Sorbini CA. Control of breathing and respiratory muscle strength in patients with multiple sclerosis. *Chest.* Apr 1994;105(4):1163-1170.
- Theodoros DG, Murdoch BE, Ward EC. Laryngeal and respiratory dysfunction in multiple sclerosis. In: Murdoch BE, Theodoros DG, eds. *Speech and Language Disorders in Multiple Sclerosis*. 1st ed. London and Philadelphia: Whurr Publishers; 2000.
- Twomey JA, Espir ML. Paroxysmal symptoms as the first manifestations of multiple sclerosis. *J Neurol Neurosurg Psychiatry.* Apr 1980;43(4):296-304.
- Van Klaveren R, Buyse T, Van De Gaer L, Meekers J, Rochette F, Demedts M. Micturitional disturbances are associated with impaired breathing control in multiple sclerosis. *Chest.* Jun 1999;115(6):1539-1545.

References on Respiratory Muscle

- Vaz Fragoso CA, Wirz D, Mashman J. Establishing a physiological basis to multiple sclerosis-related fatigue: a case report. *Arch Phys Med Rehabil.* Jun 1995;76(6):583-586.
- Wiens ME, Reimer MA, Guyn HL. Music therapy as a treatment method for improving respiratory muscle strength in patients with advanced multiple sclerosis: a pilot study. *Rehabil Nurs.* Mar-Apr 1999;24(2):74-80.
- Yamamoto T, Imai T, Yamasaki M. Acute ventilatory failure in multiple sclerosis. *J Neurol Sci.* Feb 1989;89(2-3):313-324.