Original article:

Evaluation of Brainstem Auditory Evoked Potentials in stable patients with COPD

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Abstract:

Introduction: Aim of our study is to evaluate Brainstem Auditory Evoked Potentials in stable patients with COPD.

Material &methods: in this study, 100 subjects were included: 50 Stable COPD patients with no clinical neuropathy; 50 age matched healthy volunteers as control groups. BAEP waves were recorded and compared in both the groups.

Results: We observed significantly prolonged latencies of waves III over right side and waves II & III over left side. We also observed significantly prolonged Interpeak latencies of I – III over right side and waves I - III over left side.

Conclusion: we observed significant BAEP abnormalities in the stable COPD patients with no clinical neuropathy.

Keywords: Chronic Obstructive PulmonaryDisease (COPD) ,Brainstem Evoked Response Audiometry (BERA) , Brainstem Auditory Evoked Potential (BAEP)

Introduction:

Chronic obstructive pulmonary disease (COPD) is a life-threatening lung disease that interferes with normal breathing .It is a major cause of health care burden worldwide. It is characterized by airflow limitation which is irreversible and progressive. It is due to inflammatory response of the lungs to noxious gases.Brainstem auditory evoked potentials are the potentials recorded from the ear and vertex in response to brief auditory stimulation to assess the conduction through auditory pathway. This study is to evaluate BAEP abnormalities in stable COPD patients having no clinical auditory dysfunction.

Aim and Objective of the study:

To evaluate Brainstem Auditory Evoked Potential in stable patients with Chronic Obstructive Pulmonary Disease.To find out the clinical utility of BAEP as an investigating tool in diagnosing sub-clinical involvement of auditory pathway in stable patients with COPD. The outcome of this study would help for the early diagnosis of involvement of auditory pathway in COPD patients, which may help to reduce the morbidity in COPD patients.

Material & methods:

A cross-sectional study was done in the department of physiology and experimental Medicine, govt. kilpauk medical college, Chennai with 50 stable COPD patients in the age group > 40 years with duration of illness > 5 years. The diagnosis of COPD was based on the GOLD criteria for COPD. Patients were referred from the Department of Medicine, Kilpauk Medical College. 50 age and sex matched healthy controls with no smoking

history were taken from among the staff of kilpauk medical college.

Patients with Pulmonary tuberculosis, Diabetes mellitus, Hypertension, Alcoholism, Neurological disorders, Kyphoscoliosis, Anemia, Vitamin deficiencies, Drugs causing neuropathies, Thyroid disorders, Acute severe COPD, and Bronchial asthma were excluded from the study. The study was approved by the Institutional Ethical Committee, Kilpauk Medical College.All pre-request for ethical clearance were followed.

BAEP studies were carried out on a computerized nerve conduction testing equipment : Medicaid Computerized PhysiolabNeuroperfect Plus. The signals were picked by the electrodes and were filtered, amplified, averaged, displayed on the screen of the Medicaid computerized Physiolab Neuroperfect plus and recorded. The normal BAEP recordings consists of 5 or more vertex positive waves (which were labeled by roman numericals) arising within 10 ms of auditory stimulus. Latencies of waves I,II, III,IV and V together with inter Peak latencies(IPL) of I –III, I – V, III- V were measured from recordings. Any deviations from the normal values are considered as abnormal.

Statistical analysis:

Results were derived by statistical analysis of the data obtained, and expressed in tables and charts.. The data were analyzed using SPSS 7.5 for windows student version software. The data were analyzed using independent samples t-test. P value <0.05 was considered significant. P value <0.01 was considered highly significant. P value <0.001 was considered very highly significant.

Results:

TABLE – 1

Comparison of age, height, weight and BMI between cases and controls

Variable	Group	Numbers	Mean	S.D	P value
Age	Case	50	50.12	5.752	0.145
	Control	50	51.72	5.131	
Height	Case	50	1.6986	0.06105	0.857
	Control	50	1.7008	0.06044	
Weight	Case	50	69.82	5.185	0.537
	Control	5	69.20	4.806	
BMI	Case	50	24.2106	1.45328	0.270
	Control	50	23.8828	1.50071	

There is no significant difference between cases and controls in respect to age, height, weight and BMI.

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TABLE – 2

Comparison of BAEP waves between cases and controls

RIGHT SIDE

Waves	Group	Mean	Std.Deviation	P value
I	Case	1.7762	0.059792	0.4876
	Control	1.7674	0.066327	
II	Case	2.8812	0.053667	0.3328
	Control	2.869	0.070545	
III	Case	4.2726	0.249659	<0.001*
	Control	3.9868	0.065167	
IV	Case	5.0766	0.156904	0.6106
	Control	5.0608	0.15238	
V	Case	5.7554	0.124576	0.5501
	Control	5.7388	0.150965	

* - Significant

TABLE – 3

Comparison of BAEP InterPeakLatency between cases and controls

RIGHT SIDE

Waves	Group	Mean	Std.Deviation	P value
I – III	Case	2.4964	0.260281	<0.001*
	Control	2.2194	0.10011	
III – V	Case	1.4828	0.290777	<0.002
	Control	1.7518	0.141907	
I – V	Case	3.9792	0.139604	0.7989
	Control	3.9712	0.171864	

* - Significant

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TABLE – 4

Comparison of BAEP waves between cases and controls

LEFT SIDE

Waves	Group	Mean	Std.Deviation	P value
I	Case	1.7768	0.045376	0.0546
	Control	1.7548	0.065846	
II	Case	2.9858	0.102282	<0.001*
	Control	2.8836	0.052168	
III	Case	4.1456	0.159081	<0.001*
	Control	3.9918	0.064037	
IV	Case	5.0902	0.136971	0.5732
	Control	5.1058	0.139007	
V	Case	5.7674	0.252553	0.7518
	Control	5.754	0.15954	

* - Significant

TABLE – 5

Comparison of BAEP InterPeakLatency between cases and controls

LEFT SIDE

Waves	Group	Mean	Std.Deviation	P value
I – III	Case	2.3688	0.163366	<0.001*
	Control	2.2276	0.097845	
III – V	Case	1.6218	0.121918	<0.002
	Control	1.7716	0.192389	
I – V	Case	3.9906	0.251148	0.8398
	Control	3.9992	0.164278	

* - Significant

Discussion:

This study was done to evaluate Brainstem Auditory Evoked Potential in stable patients with Chronic Obstructive Pulmonary Disease and to find out the clinical utility of BAEP as an investigating tool in diagnosing sub-clinical involvement of auditory pathway in stable patients with COPD. The outcome of this study would help for the early diagnosis of involvement of auditory pathway in COPD patients, which may help to reduce the morbidity in COPD patients.

Our study consists of a total sample size of 100 subjects which includes 50 stable COPD patients and 50 age matched healthy controls.

Table- 1 shows that there is no significant difference between cases and controls in respect to age, height, weight and BMI in our study.In our study, the mean age of the control group was 51.72 ± 5.131 years ranging from 40 to 60 years, and the

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mean age of the COPD patients was 50.12 ± 5.752 years ranging from 40 to 60 years. P value is 0.145(not statistically significant). There was no significant difference in the mean age between cases and controls.

In our study, COPD patients with duration of illness 5 years and above were selected. In our study, the mean height of the control group was 1.7008 ± 0.06044 meters. The mean height of the COPD patients was 1.6986 ± 0.06105 meters. P value is 0.857 (not statistically significant). There was no significant difference in the mean height between cases and controls. In our study, the mean weight of the control group was 69.20 ± 4.806 kg. The mean weight of the COPD patients was 69.82 ± 5.185 kg. P value is 0.537 (not statistically significant). There was no significant difference in the mean weight between cases and controls. In our study, the mean BMI of the control group was 23.8828 ± 1.50071. The mean BMI of the COPD patients was 24.2106 ± 1.45328. P value is 0.270 (not statistically significant). There was no significant difference in the mean BMI between cases and controls.

In our study, the mean value of wave I latency on the right side was 1.7762 ± 0.059792 milliseconds and 1.7674 ± 0.066327 milliseconds respectively in cases and controls. P value is 0.4876 (not statistically significant).

In our study, the mean value of wave II latency on the right side was 2.8812 ± 0.053667 milliseconds and 2.869 ± 0.070545 milliseconds respectively in cases and controls. P value is 0.3328 (not statistically significant).

In our study, the mean value of wave III latency on the right side was 4.2726 ± 0.249659 milliseconds and 3.9868 ± 0.065167 milliseconds respectively in cases and controls. P value is < 0.001
(statistically significant).

In our study, the mean value of wave IV latency on the right side was 5.0766 ± 0.156904 milliseconds and 5.0608 ± 0.15238 milliseconds respectively in cases and controls. P value is 0.6106 (not statistically significant).

In our study, the mean value of wave V latency on the right side was 5.7554 ± 0.124576 milliseconds and 5.7388 ± 0.150965 milliseconds respectively in cases and controls. P value is 0.5501 (not statistically significant).

In our study, the mean value of wave I - III latency on the right side was 2.4964 ± 0.260281 milliseconds and 2.2194 ± 0.10011 milliseconds respectively in cases and controls. P value is < 0.001 (statistically significant).

In our study, the mean value of wave III - V latency on the right side was 1.4828 ± 0.290777 milliseconds and 1.7518 ± 0.141907 milliseconds respectively in cases and controls. P value is < 0.002 (not statistically significant).

In our study, the mean value of wave I - V latency on the right side was 3.9792 ± 0.139604 milliseconds and 3.9712 ± 0.171864 milliseconds respectively in cases and controls. P value is 0.7989 (not statistically significant).

In our study, the mean value of wave I latency on the left side was 1.7768 ± 0.045376 milliseconds and 1.7548 ± 0.065846 milliseconds respectively in cases and controls. P value is 0.0546 (not statistically significant).

In our study, the mean value of wave II latency on the left side was 2.9858 ± 0.102282 milliseconds and 2.8836 ± 0.052168 milliseconds respectively in cases and controls. P value is < 0.001
(statistically significant).

In our study, the mean value of wave III latency on the left side was 4.1456 ± 0.159081 milliseconds and 3.9918 ± 0.064037 milliseconds respectively in cases and controls. P value is < 0.001
(statistically significant).

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In our study, the mean value of wave IV latency on the left side was 5.0902 ± 0.136971 milliseconds and 5.1058 ± 0.139007 milliseconds respectively in cases and controls. P value is 0.5732 (not statistically significant).

In our study, the mean value of wave V latency on the left side was 5.7674 ± 0.252553 milliseconds and 5.754 ± 0.15954 milliseconds respectively in cases and controls. P value is 0.7518 (not statistically significant).

In our study, the mean value of wave I - III latency on the left side was 2.3688 ± 0.163366 milliseconds and 2.2276 ± 0.097845 milliseconds respectively in cases and controls. P value is < 0.001 (statistically significant).

In our study, the mean value of wave III - V latency on the left side was 1.6218 ± 0.121918 milliseconds and 1.7716 ± 0.192389 milliseconds respectively in cases and controls. P value is < 0.002 (not statistically significant).

In our study, the mean value of wave I - V latency on the left side was 3.9906 ± 0.251148 milliseconds and 3.9992 ± 0.164278 milliseconds respectively in cases and controls. P value is 0.7989 (not statistically significant).

To summarize, in the present study we included 50 stable COPD patients and 50 age matched healthy controls. Latencies of BAEP waves I,II,III,IV,V and Interpeak latencies (IPL) I –III, III – V, I – V were studied in both the groups. We observed significantly prolonged latencies of waves III over right side and waves II & III over left side. We also observed significantly prolonged Interpeak latencies of I – III over right side and waves I - III over left side.

Conclusion:

To conclude, in the present study, we observed significant BAEP abnormalities on electrophysiological evaluation in the stable COPD patients with mild to moderate airflow obstruction and with no clinical neuropathy, which may be due to chronic hypoxemia. The reasons for the chronic hypoxemia could be disease pathology itself, tobacco smoking,drugs used in COPD like inhaled β2 agonist, inhaled anticholinergic agents, inhaled glucocorticoids, and theophylline. **On the right side** there is significant prolongation of absolute latencies of wave III and Interpeak latency of I – III. There is no significant difference in latencies of waves I,II,IV,V and IPL III-V, I – V between stable COPD patients and controls. **On the left side** there is significant prolongation of absolute latencies of wave II,III and Interpeak latency of I – III. There is no significant difference in latencies of waves I,,IV,V and IPL III-V, I– V between stable COPD patients and controls.This study proves that Brainstem Auditory Evoked Potentials can be used as an investigatory tool to identify subclinical involvement of auditory pathways in stable COPD patients with mild to moderate airway obstruction.Further studies are needed to better define the reason for auditory pathway involvement in COPD patients , which may help to reduce the morbidity of COPD patients.

References:

1. Adrain ED, Mathews BHC. The Berger rhythm: Potential changes from occipital lobes in man. Brain 1934; 57: 356.

2.AgarwalD,VohraR,GuptaPP,SoodS;Dept of Physiology, Postgraduate Istitute of Medical Sciences, Rohtak ,India; Subclinical peripheral neuropathy in stable COPD patients;Singapore Med J.2007 oct;48(10);887-94.

3. American thoracicv society. Standards for diagnosis and care of patients with chronic obstructive pulmonary disease and asthma. Am Rev Respir Dis.1987;163:225-44.

4. Atiff S, OzgeA,SevimS;Dept of chest disease,MersinUniversity,Faculty of Medicine,Icel,Turkey;Abnormalities of auditory evoked potentials in severe COPD patients;Respirology,2001,sep;6(3):225-9.

5.Barbieri S, FayoumiZ,BerardinelliP,CappellariA,CavestroC,ValliG,ScarlatoG;Institute of clinical neurology, University of Milan, Italy;Evidence for a subclinical involvement of the central nervous system in mild or moderate chronic respiratory insufficiency; ElectromyogrClinNeurophysiol. 1996 Mar;36(2);67-72.

6. Barker AT, JalinousR.Freeston IL. Noninvasive magnetic stimulation of human motor cortex. Lancet 1985; 2: 1106.

7. Barr RG, Rowe BH, Camargo CA (2003)."Methylxanthines for exacerbations of chronic obstructive pulmonary disease".In Barr, R Graham. *Cochrane Database Syst Rev* (2): CD002168.

8. Braddom RL, Schuchmann J. Motor conduction. In Jonhson FW (Ed.) Practical Electromyography. Williams and wilkins, Baltimore, 1989, P.46.

9. Brazier MAB. Emergence of electrophysiology as an aid to neurology. In: Aminoff MJ (Ed.), Electrodiagnosis in Clinical Neurology. Churchill Livingstone, New York, 1980, p.1.

10. Brown WP. Needle electromyographic abnormalities in neurogenic and myogenic disease. In: Brown WF (Ed.) The physiological and Technical Basis of Electromyography. Butterworth, Stoneham, 1984, p.317.

11. Buchthal F, Guld C, Rosenfalck P. Action Potential parameters in normal human muscle and their dependence on physical variables ActaPhysiolScand 1954; 34: 200.

12. Calverley PM, Koulouris NG (2005). "Flow limitation and dynamic hyperinflation: key concepts in modern respiratory physiology". *EurRespir J* 25 (1): 186–199.

13.Calverley PM, Anderson JA, Celli B et al. (2007). "Salmeterol and fluticasone propionate and survival in chronic obstructive pulmonary disease". *N. Engl. J. Med.* 356 (8): 775–89.

14. Campbell WW. Ward LC, Swift TR. Nerve Conduction velocity varies inversely with height. Muscle Nerve 1980; 3 : 436.

15. Carlucci A, Guerrieri A, Nava S (December 2012). "Palliative care in COPD patients: is it only an end-of-life issue?". *EurRespir Rev* 21 (126): 347–54.

16. Celli BR, Cote CG, Marin JM et al. (March 2004). "The body-mass index, airflow obstruction, dyspnea, and exercise capacity index in chronic obstructive pulmonary disease". *N. Engl. J. Med.* 350 (10): 1005-12.

17.Chiappa KH. Evoked Potentials in Clinical Medicine, 2nd ed. Raven Press, New York, 1990.

18. Chiappa KH, Gladstone KJ, Young RR, Brainstem auditory evoked response: studies of waveform variation in fifty normal human subjects.ArchNeurol 1979;36:81.

19. Chiappa KH, Parker SW. A simple needle electrode technique for improved registration of wave I in brainstem auditory evoked potentials. In: Starr A, Rosenberg C, Don M, Davis H (Eds.),sensory evoked potentials,151 International Conference on standards in auditory brainstem response testing, 1984, p.137.

20. Chiappa KH, Physiologic localization using evoked responses; pattern shift visual , brainstem auditory and short latency somatosensory. In: Thompson RA, Green JR(Eds.), New Perspective in Cerebral localization. Raven Press, NewYork, 1982, p.63.

21. "COPD (Chronic Obstructive Pulmonary Disease)".*Educational Campaigns*. National Heart, Lung, and Blood Institute, U.S. Department of Health & Human Services. 2012-02-15. Retrieved 2013-07-23. "2007 NHLBI Morbidity and Mortality Chart Book" (PDF).Retrieved 2008-06-06.

22. "COPD — Treatment". U.S. National Heart Lung and Blood Institute. Retrieved 2013-07-23

23. Cueva RA, Auditory brainstem response versus magnetic resonance imaging for the evaluation of asymmetric sensorineural hearing loss. Laryngoscope 2004; 114: 1686.

24. Dan L.Lango,MD,DennisL.Kasper,MD,J.LarryJameson,MD, Antony S.Fauci,MD, Stephen L.Hauser,MD, Joseph Loscalzo,MD,PhD: Harrison"s Principles of Internal Medicine vol II,18 th E : COPD

25. Dawson GD. Cerebral response to electrical stimulation of peripheral nerve in man. J.NeurolNeurosurgpsychiat 1947; 10:137.

26. Dawson GD. A summation technique for the detection of small evoked potentials.ElectroencephalogrClinNeurophysiol 1954; 6.65.

27. Dawson GD. Relative excitability and conduction velocity of sensory and motor nerve fibres in man. J Physiol (Lond) 1956; 131: 436.

28. Decramer M, Janssens W, Miravitlles M (April 2012). "Chronic obstructive pulmonary disease". *Lancet* 379 (9823): 1341–51.

29. Decramer, ML; Hanania, NA; Lötvall, JO; Yawn, BP (2013). "The safety of long-acting β2-agonists in the treatment of stable chronic obstructive pulmonary disease.". *International journal of chronic obstructive pulmonary disease* 8: 53–64.

30. "Definition of pack year". *NCI Dictionary of Cancer Terms*.

31. Devereux, G (2006 May 13). "ABC of chronic obstructive pulmonary disease. Definition, epidemiology, and risk factors.".*BMJ (Clinical research ed.)* 332 (7550): 1142–4.

32. Donohoe CD, Application of brainstem auditory evoked response in clinical neurologic practice . In: Owen JH, Donohoe CD (Eds.), Clinical Atlas of auditory evoked potentials. Grune and Stratton, New York, 1988.

33. Drummond MB, Dasenbrook EC, Pitz MW, Murphy DJ, Fan E (November 2008). "Inhaled corticosteroids in patients with stable chronic obstructive pulmonary disease: a systematic review and meta-analysis". *JAMA* 300 (20): 2407–16.

34. Dumitru d. Walsh N. Practical instrumentation and common sources of error. Am J Phys Med Rehabil 1988; 67:55.

35. Emerson RG,BrooksEB,ParkerSW,et al. Effects of click polarity on brainstem auditory evoked potentials in normal subjects &patients;Ann NY AcadSci 1982;388:710.

36. Fishman AP (May 2005). "One hundred years of chronic obstructive pulmonary disease". *Am. J. Respir. Crit. Care Med.*171 (9): 941–8.

37. Galvani L, DeViribus. Electricitatis in motor musculari comment arius. De Bononiensiscientiarumet Atrium InstitutoatqueAcadimiaCommentarii 1791; 7: 363.

38. Gartlehner G, Hansen RA, Carson SS, Lohr KN (2006). "Efficacy and Safety of Inhaled Corticosteroids in Patients With COPD: A Systematic Review and Meta-Analysis of Health Outcomes". *Ann Fam Med* 4 (3): 253–62.

39. Gassel MM. Sources of error in motor nerve conduction studies. Neurology (Minneap) 1964; 14: 825.

40. Georges Juvelekian, James K. Stoller, Chronic Obstructive Pulmonary Disease,LungSummit:Advances in pulmonary Medicine,critical care Medicine, and Mechanical Ventilation;sep25-27,2013;Cleveland,Ohio.

41. Global strategy for the diagnosis,management and prevention of chronic obstructive pulmonary disease : $NHLB_1$ /WHO workshop report.Bethesda,MD,US:NIH Publication no 2701;2004. Global Initiative for chronic obstructive pulmonary disease;pp 1-112.

42. Gitter AJ, Stolov WC. AAEM monograph # 16: instrumentation and measurement in electrodiagnostic medicine. Part I, Muscle Nerve 1995; 18: 799.

43. Gitter AJ. Stolov WC. AAEM monograph # 16 instrumentation and measurement in electrodiagnostic medicine. Part II Muscle Nerve 1995; 18: 812.

44. Gupta PP,AgarwalD,chronic obstructive pulmonary disease and peripheral neuropathy.Lung India;2006;23:25-33.

45. Guyton and Hall, Textbook of Medical Physiology, Abnormal V_A/Q in COPD,12 ed.,p494.

46. Halbert RJ, Natoli JL, Gano A, Badamgarav E, Buist AS, Mannino DM (September 2006). "Global burden of COPD: systematic review and meta-analysis". *Eur. Respir. J.* 28 (3): 523–32.

47. Hammond SR, Yiannikas C, Chan YW. A comparison of brainstem auditory evoked responses evoked by rarefaction and condensation stimulation, J NeurolSci 1986; 74: 177.

48. Helmholtz H.VorlaufigerBerichuber die Fortpflanzungs- geschwindigkeit der nervenreizung. Arch AnatPhysiolWiss Med 1850; 71, 185.

49. Hermann L Untersuchungenuber die Actionsstrome des Muskels, pflugers. Arch GesPhysiol 1878; 16: 191.

50. Hnizdo E, Vallyathan V (April 2003). "Chronic obstructive pulmonary disease due to occupational exposure to silica dust: a review of epidemiological and pathological evidence". *Occup Environ Med* 60 (4): 237–43.

51. Holland, AE; Hill, CJ; Jones, AY; McDonald, CF (2012 October 17). "Breathing exercises for chronic obstructive pulmonary disease.".In Holland, Anne E. *The Cochrane database of systematic reviews* 10: CD008250.

52. Humboldt FA. VersucheUber die gereizteMuskelundNervenfasernebstVermutungeuber den chemischen process Lebns in der Their und ptlanzenwelt, Vol.2, Decer, Posen, und Rottman, Berlin, 1797.,

53. Hunninghake GM et al: MMP12, lung function, and COPD in high risk populations. N Engl J Med 361:2599,2009.

54. Ito K et al : Decreased histone deacetylase activity in chronic obstructive pulmonary disease. N Eng J Med 352:1967,2005.

55. John J.Reilly et al,Chronic obstructive Pulmonary Disease, Harrison"s Principles of Internal Medicine, 18^{th}e, p2151-60.

56. Journal of thoracic disease,vol 4,No 3,june 2012,review article,COPD in India.

57. Kayacan O, BederS,DedaG,Karnak D;;Ankara University Medical Faculty, Dept. of Chest DiseasesandTuberculosis;Ankara,Turkey;Neurophysiological changes in COPD patients; ActaNeurol Belg;2001;sep;101(3);160-5.

58. Kennedy SM, Chambers R, Du W, Dimich-Ward H (December 2007). "Environmental and occupational exposures: do they affect chronic obstructive pulmonary disease differently in women and men?". Proceedings of the American Thoracic Society 4 (8): 692–4.

59. Lacasse Y, Brosseau L, Milne S et al. (2002*).* "Pulmonary rehabilitation for chronic obstructive pulmonary disease".In Lacasse, Yves. Cochrane database of systematic reviews (Online) (3): CD003793.

60. Liesker JJ, Wijkstra PJ, Ten Hacken NH, Koëter GH, Postma DS, Kerstjens HA (February 2002). "A systematic review of the effects of bronchodilators on exercise capacity in patients with COPD". *Chest* 121 (2): 597–608.

61. Loscalzo, Joseph; Fauci, Anthony S.; Braunwald, Eugene; Dennis L. Kasper; Hauser, Stephen L; Longo, Dan L. (2008).*Harrison's Principles of Internal Medicine* (17th ed.).

62. Louis AA, Hotson JR. Regional cooling of human nerve and slowed NA^+ inactivation. ElectroencephalogrClinNeurophysiol 1986; 63: 371.

63. Macintyre NR: Mechanism of functional loss in patients with chronic lung disease,Respir Care 53:1177,2008.

64. Maynard F, StolovW.Experimental error in determination of nerve conduction velocity. Arch Phys Med Rehabil 1972; 53: 362.

65. McKay AJ, Mahesh PA, Fordham JZ, Majeed A. Prim Care Respir J. 2012 Sep;21(3):313-21. Prevalence of COPD in India: a systematic review .

66. MagendieF.Process – Verb.AcadSci 1822; 7: 348

67. Mahler DA (2006). "Mechanisms and measurement of dyspnea in chronic obstructive pulmonary disease".*Proceedings of the American Thoracic Society* 3 (3): 234–8.

68. Mammen, MJ; Sethi, S (2012). "Macrolide therapy for the prevention of acute exacerbations in chronic obstructive pulmonary disease.". *PolskieArchiwumMedycyny Wewnetrznej*122 (1-2): 54–9.

69. Mannino DM, Buist AS: Global burden of COPD: Risk factors, prevalence, and future trends. Lancet 370: 765, 2007.

70. Marinkovic, D; Aleksic-Kovacevic, S, Plamenac, P (2007). "Cellular basis of chronic obstructive pulmonary disease in horses". *International review of cytology*. International Review of Cytology 257: 213–15.

71. MatteucciC.Surunphenomenicphysiologuiqeproduit par les muscles en contraction. Ann Chimie physique 1842; 6:339.

72. MatteucciC.Traite des phenomeneselectrophysiolo'giques – des Animaux. Fortin, Masson, Paris, 1844.

73. Merton PA Morton HB. Stimulation of cerebral cortex in intact human subject. Nature 1980; 285: 287.

74. Murray, CJ (2012 Dec 15). "Disability-adjusted life years (DALYs) for 291 diseases and injuries in 21 regions, 1990-2010: a systematic analysis for the Global Burden of Disease Study 2010.". *Lancet* 380 (9859): 2197–223.

75. Nandekar SD, Sanders DB, Recording characteristics of monopolar needles. Muscle Nerve 1991; 14: 108.

76. Murthy KJR et al NCMH Background Papers,2005.

77. Nathell, L.; Nathell, M.; Malmberg, P.; Larsson, K. (2007). "COPD diagnosis related to different guidelines and spirometry techniques". *Respiratory research* 8 (1): 89.

78. National Institute for Health and Clinical Excellence. *Clinical guideline 101: Chronic Obstructive Pulmonary Disease*. London, June 2010.

79. Newer MR, Aminoff M, Goodin D, et al. IFCN recommended standards for brainstem auditory evoked potentials .Report of IFCN committee.ElectroencephalogrClinNeurophysiol 1994; 91:12.

80. Nobili L. AnalyseExperimentaleettheorique des phenomenisphysiologiques products par electric sur la grenouile; avee un appendicesur la nature du tetanous et da la paralysi et sur less moyens de tritercesdwx maladies par I' electric. Ann Chemie physique Series 2, 1830; 44: 60.

81. Norris AH, Shock, NW, Wagman IH. Age changes in the maximum condction velocity of motor fibres of human ulnar nerve. J ApplPhysiol 1953; 5: 589.

82. Ochs S, Brimijoin WS. Axonal transport. In: Dyck PJ. Thomas PK, Griffin JW, et al (Eds) Peripheral Neuropathy, 3rd ed. WB Saunders, Philadelphia, 1993, P.331

83. O'Donnell DE (2006). "Hyperinflation, Dyspnea, and Exercise Intolerance in Chronic Obstructive Pulmonary Disease". *The Proceedings of the American Thoracic Society* 3 (2): 180–4.

84. Petty TL (2006). "The history of COPD". *Int J Chron Obstruct Pulmon Dis* 1 (1): 3–14.

85. Pfeiffer G,KunzeK,BruchM,KutzerM,LadurnerG,MalinJP,TackmannW;Dept of Neurology,Universitatsklinik Hamburg Eppendorf, Federal Republic of Germany; Polyneuropathy associated with chronic hypoxaemia in COPD patients; J Neurol.1990, July;237(4);230-3.

86. PictonTW,Stapells DR, Campbell KB.Auditory evoked potentials from human cochlea and brainstem.Jotolaryngol 1981;9(s):1.

87. "Pink Puffer - definition of Pink Puffer in the Medical dictionary - by the Free Online Medical Dictionary, Thesaurus and Encyclopedia". Medical-dictionary.thefreedictionary.com. Retrieved 2013-07-23.

88. PremPrakashGuptha,SushmaSood,AtulyaAtreja, andDiptiAgarwal; Auditory evoked potential in COPD patients; Annals of Thoracic Medicine;2008 ;oct-dec;3(4);128-134.

89. Puhan MA, Gimeno-Santos E, Scharplatz M, Troosters T, Walters EH, Steurer J (2011). "Pulmonary rehabilitation following exacerbations of chronic obstructive pulmonary disease".In Puhan, Milo A. *Cochrane Database Syst Rev* (10): CD005305.

90. Rabe KF, Hurd S, Anzueto A et al. (2007)."Global Strategy for the Diagnosis, Management, and Prevention of Chronic Obstructive Pulmonary Disease: GOLD Executive Summary". *Am. J. Respir. Crit. Care Med.* 176 (6): 532–55.

91. Raghev T. Geddes LA. Electrical properties of metallic electrodes. Med BiolEngComput 1990; 28: 182.

92. Rennard SI, Fogarty C, Kelsen S et al. (May 2007). "The safety and efficacy of infliximab in moderate to severe chronic obstructive pulmonary disease". *Am. J. Respir. Crit. Care Med.*175 (9): 926–34.

93. Rennard, S. I.; Vestbo, J. R. (2006). "COPD: the dangerous underestimate of 15%". *The Lancet* 367 (9518): 1216.

94. Rossini PM, Caramia MD Methodological and Physiological consideration on electric and magnetic transcranial stimulation. In Non Invasive Stimulation of Brain and Spinal Cord; Fundamentals and Clinical Application.Alan r Liss, New York, 1988, 36.

95. Sarlandier C. Memories sur I' electro – Puncture. L' Auteur and M. Delaunay, Prais, 1825.

96. Shafazand, S (2013 Jun 18). "Review: Inhaled medications vary substantively in their effects on mortality in COPD.". *Annals of internal medicine* 158.

97. Simpson CR, Hippisley-Cox J, Sheikh A (2010). "Trends in the epidemiology of chronic obstructive pulmonary disease in England: a national study of 51 804 patients". *Brit J Gen Pract*60 (576): 483–8.

98. Simpson JA. Fact and fallacy in measurement of Velocity in motor nerves. J. NeurolNeurosurgPsychiat 1964; 27: 381.

99. Sin DD et al : Inhaled corticosteroids and mortality in chronic obstructive pulmonary disease. Thorax 60: 992, 2005.

100. SohmerH,FreemanS,MalachiS.Multimodality evoked potentials in hypoxemia. ElectroencephalogrClin Neurophysiol.1986;64:328-33.

101. Stockard JJ, Stockard JE, Sharbrough FW. Nonpathological factors influencing brainstem auditory evoked potentials. Am J EEG Technol 1978; 18: 177.

102. Stockard JJ, Stockard JE, Sharbrough FW. Brainstem auditory evoked potentials in neurology:methodology,interpretation and clinical application. In:Aminoff MJ (Ed), electrodiagnosis in clinical neurology. Churchill Livingstone,Newyork,1986.

103. Stockard JJ, Stockard JE, Westmoreland BF, et al. Brainstem auditory evoked responses; normal variation as a function of stimulus and subject characteristics. Arch Neurol 1979; 36: 823.

104. Surinder K. Jindal, Review Article Indian J Med Res 124, December 2006, pp 619-630 Emergence of chronic obstructive pulmonary disease as an epidemic in India. Department of Pulmonary Medicine, Postgraduate Institute of Medical Education & Research Chandigarh, India.

105. Taylor PK. Nonlinear effects of age of nerve conduction in adjlts J. NeurolSci 1984; 66: 223.

106. "The Global Initiative for Chronic Obstructive Lung Disease (GOLD)". Retrieved 15 June 2013.

107. UK Misra , J Kalita . Clinical Neurology 2e;New Delhi ; Elsevier,Reed Elsevier India Pvt Ltd 2o11;pg.329-346.

108. Vestbo, Jorgen (2013). *Global Strategy for the Diagnosis, Management, and Prevention of Chronic Obstructive Pulmonary Disease*.Global Initiative for Chronic Obstructive Lung Disease. p. Chapter 2.

109. Vos, T (2012 Dec 15). "Years lived with disability (YLDs) for 1160 sequelae of 289 diseases and injuries 1990-2010: a systematic analysis for the Global Burden of Disease Study 2010.". *Lancet* 380 (9859): 2163–96.

110. "What Are the Signs and Symptoms of COPD?".U.S. National Heart Lung and Blood Institute. 8 June 2012.

111. WHO,Chronic obstructive pulmonary disease (COPD) Fact sheet No 315 November 2012

112. WHO,"The 10 leading causes of death in the world, 2000 and 2011". July 2013. Fact sheet No 310.

113."World Health Organization Tobacco Free Initiative — Policy recommendations for smoking cessation and treatment of tobacco dependence". Retrieved 28 July 2008.

114. Wise RA, Tashkin DP: Optimizing treatment of chronic obstructive pulmonary disease: An assessment of current therapies. Am J Med 120: S4, 2007.

115. Wright, Joanne L.; Churg, Andrew (2008). "History of pathologic descriptions of COPD".In Fishman, Alfred; Elias, Jack; Fishman, Jay. *Fishman's Pulmonary Diseases and Disorders* (PDF) (4th ed.). McGraw Hill Professional. pp. 693–705.

116. Young RP, Hopkins RJ, Christmas T, Black PN, Metcalf P, Gamble GD (August 2009). "COPD prevalence is increased in lung cancer, independent of age, sex and smoking history". *Eur. Respir. J.* 34 (2): 380–6.

117. Ziemssen H. Die Electriciat in der Medicine. August Hirschwald, Berlin. 1866.

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