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Multiple Sclerosis Diagnosis by Flow Cytometry

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Commentary

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Introduction

Multiple sclerosis (MS) is the prototypic neuroinflammatory disease, defined by neuroinflammation within the central nervous system (CNS) accompanied by demyelination and axonal disruption [1-3]. Here, the diagnostic tool "Flow Cytometry" is used to analyze the physical and chemical characteristics disorders in MS. Flow cytometry is a widely used high-throughput measurement technology in basic research and diagnostics [3-6].

Multiple Sclerosis (MS) is an inflammatory disease of nervous system where it disrupts the insulating cover of nerves in brain and spinal cord resulting disability of the parts of the nervous system to communicate [7-10]. Any imbalance results physical, mental and sometimes psychological problems may also occur. The mysterious nature of disease provides wide-ranging scope for research. Coming to diagnostic challenges, neuroimaging advent, therapeutic options, and pathobiological research advancement in multiple sclerosis patients have been informed by many new insights from past few years [11-15].

This neuroinflammatory malady that influences myelin, a substance that makes up the film (called the myelin sheath) that wraps around nerve strands (axons). Myelinated axons are ordinarily called white matter. Scientists have discovered that MS additionally harms the nerve cell bodies, which are found in the cerebrum's dark matter, and also the axons themselves in the mind, spinal line, and optic nerve (the nerve that transmits visual data from the eye to the cerebrum). As the infection advances, the cerebrum's cortex contracts (cortical decay) [16-21].

The term Multiple sclerosis alludes to the particular regions of scar tissue (sclerosis or plaques) that are obvious in the white matter of individuals who have MS. Plaques can be as little as a pinhead or as extensive as the extent of a golf ball. Specialists can see these zones by inspecting the mind and spinal string utilizing a sort of cerebrum output called attractive reverberation imaging (MRI) [22-24]. While MS in some cases causes extreme disability, it is just seldom deadly and the vast majority with MS has a typical future [25-26].

MS is the most common neurological condition among young adults diagnosed usually between the ages of 20-24. This is at a stage in life when people are starting their journey in the world of employment, a time of seeking

independence. Being diagnosed with MS produces a myriad of challenges not least of which is 'can one continue to work?'^[27-35]

MS Diagnosis?

There is no single test used to analyze MS. Specialists utilize various tests to discount or affirm the conclusion. There are numerous different issues that can copy MS. Some of this different issue can be cured, while others require diverse medications than those utilized for MS. Along these lines it is critical to perform an intensive examination before making a finding^[36-39].

Notwithstanding a complete therapeutic history, physical examination, and a definite neurological examination, a specialist will arrange a MRI sweep of the head and spine to search for the trademark injuries of MS. X-ray is utilized to produce pictures of the cerebrum and/or spinal line. At that point an exceptional color or complexity operators is infused into a vein and the MRI is rehashed. In districts with dynamic aggravation in MS, there is interruption of the blood-cerebrum obstruction and the color will spill into the dynamic MS sore^[40-45].

We know that diseases of cranial nerves are difficult to diagnose and treat. Some of the pathologies presenting clinically with symptoms, referable to cranial nerves, mostly involve them, while most others cause extraneous compression of these fine structures that traverse through a unique environment of meninges^[46-49].

There are several neurological examinations performed in general to detect this syndrome. The clinical and neurological tests includes: Flow Cytometry, MRI, spinal tap, evoked potentials etc.

In recent studies the amount of data generated from Flow Cytometry experiments has been increasing, both in sample numbers and the number of parameters measured per cell. These greatly multivariate datasets have become too large for use with tools depending mainly on manual analysis^[50-54].

Flow Cytometry technology can be used for studying both the phenotype and function of immune cells by using this technique it is used in development of a diagnostic laboratory test for the immunologic monitoring of this disease^[55-59]. Cell components are fluorescently labeled and then excited by the laser to emit light at varying wavelengths. Pathological research is an attempt to identify its type in MS patients using flow cytometry. In this study investigation the possible prognostic value of ploidy in humans and the disruptions occurring inside the cell cycle with flow cytometry is used as a diagnostic tool. Flow cytometry enables speedy quantification of DNA content of individual cells, and the cellular DNA content provides useful evidence about the ploidy, saying the modal DNA value, and the proliferative activity in a tissue. The ability of flow cytometry to estimate cellular DNA content is based on the measurement of fluorescence from dyes which bind in a stoichiometric manner to DNA. Using flow cytometry for DNA analysis between family members with genetically linked diseases provides fast results, permits multiparameter analysis correlating DNA content with antigen expression, and also provides sensitivity for detecting near-diploid aneuploid peaks^[60-65].

In recent studies on flow Cytometry provided evidence of the expression levels of the CB2R expression levels of the CB2R in different immune cell subsets. Higher levels of CB2R were detected in NK cells, B-lymphocytes and monocytes than in CD4+ or CD8+ T-lymphocytes, whereas neutrophils expressed a low level of CB2R. Furthermore, taking advantage of a sensitive technique like flow cytometry, it was observed that CB2R are present on resting T-lymphocytes at low abundance in some healthy subjects.^[66]

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technique like flow cytometry, it was observed that CB2R are present on resting T-lymphocytes at low abundance in some healthy subjects [67]

As a diagnostic tool it is used to investigate the possible prognostic value of ploidy in humans and the disruptions occurring inside the cell cycle [68]. Flow Cytometry enables rapid quantification of DNA content of individual cells, and the cellular DNA content provides helpful data roughly the ploidy, expressing the modal DNA value, and the proliferative action in a tissue. The ability of flow cytometry to evaluation cellular DNA content is based on the measurement of fluorescence from dyes which bind in a stoichiometric manner to DNA. As an analysis method it is used for the genetic analysis and the progress of the disease [69].

Flow cytometry becomes a crucial tool to monitor the immunologic effects of the drugs in MS patients. Prominently these changes might eventually be predictive of the clinical effects and the therapy outcome in MS patients [70]

White blood cell (WBC) counts in cerebrospinal fluid (CSF) are vital for the diagnosis of many neurological disorders. WBC counting and differential can be performed by microscopy, hematology analyzers, or flow cytometry. Flow cytometry of CSF is progressively being well-thought-out as the method of choice in patients suspected of leptomeningeal localization of hematological malignancies [71-74].

Technically, the low cellularity of CSF samples, joint with the rapidly declining WBC viability, makes CSF flow cytometry challenging Intracellular cytokines in peripheral blood mononuclear cells (PBMC) of MS patients by flow cytometry (cytokine flow cytometry). Flow cytometry and cytokine assay is employed to study the functional responses of the NKR⁺ T cells to stimulation with α -GalCer [75].

MS clinical phase changes remains an open question, and flow cytometry will be an indispensable tool for addressing this critical knowledge in MS.

Reference

1. Chirivi RGS, van Rosmalen JWG, Jenniskens GJ, Pruijn GJ, Raats JMH. Citrullination: A Target for Disease Intervention in Multiple Sclerosis and other Inflammatory Diseases? *J Clin Cell Immunol.* 2013; 4:146.
2. Hegazi AG, Al-Menabbawy K, Abd El Rahman E, Helal SI. Novel Therapeutic Modality Employing Apitherapy for Controlling of Multiple Sclerosis. *J Clin Cell Immunol.* 2015; 6:299.
3. Balnyte R, Rastenyte D, Vaitkus A, Uloziene I, Vitkauskiene A, et al. Associations of HLA DRB1 Alleles with Igg Oligoclonal Bands and Their Influence on Multiple Sclerosis Course and Disability Status. *J Neurol Neurophysiol.* 2015; 6:268.
4. Wens I, Broekmans T, Hendriks JJA, Savelberg HH, Hesselink MK et al. Effects of Exercise Intensity in Experimental Autoimmune Encephalomyelitis. *J Mult Scler.* 2015; 2:133.
5. Wens I, Broekmans T, Hendriks JJA, Savelberg HH, Hesselink MK, et. al. Effects of Exercise Intensity in Experimental Autoimmune Encephalomyelitis. *J Mult Scler.* 2015; 2:1
6. Abdul Mannan Baig. Mitochondrial DNA Mutation in Microglia Can Be Treated by SCNT Cloning and Not by Reprogramming of Olfactory Ensheathing Cells in the Multiple Sclerosis Treatment. *J Mult Scler* 2015; 2:1
7. Ahmed H Badawi, Paul Kiptoo and Teruna J Siahaan. Immune Tolerance Induction against Experimental Autoimmune Encephalomyelitis (EAE) Using A New PLP-B7AP Conjugate that Simultaneously Targets B7/CD28 Costimulatory Signal and TCR/MHC-II Signal. *J Mult Scler.* 2015; 2:1
8. Sushmita Sinha, Michael P. Crawford, Sterling B. Ortega and Nitin J. Karandikar. Multiparameter Flow Cytometric Assays to Quantify Effector and Regulatory T-Cell Function in Multiple Sclerosis. *J Mult Scler.* 2015; 2:130
9. Bak TH, Chandran S, Connick P. Impairment of Visual Cognition in Progressive Multiple Sclerosis. *J Mult Scler.* 2014; 1:129.
10. Bifulco M, Malfitano AM. Advances in Flow Cytometry Investigation of Cannabinoid CB2 Receptor Agonists in Multiple Sclerosis: Commentary. *J Mult Scler.* 2014; 1:128

11. Laing CM, Phillips LH, Cooper CL, Hosie JA, Summers M. Anger, Quality of Life and Mood in Multiple Sclerosis. *J Mult Scler.* 2014; 1:127.
12. Isabel Moreira and Monica Marta. New and Old Concepts and Strategies for Progressive Multifocal Leukoencephalopathy. *J Mult Scler.* 2015.
13. Arias VM, Martin SE, Farrell J, Kattah JC. Neurological Deterioration in a PML-HIV Patient in the Absence of Immune Reconstitution Inflammatory Syndrome. *J Mult Scler.* 2014; 1:125.
14. Gudesblatt M, Agashivala N, Randhawa S, Li S, Barbato L, et al. Outcomes of a Switch to Fingolimod to Treat Relapsing Multiple Sclerosis: A Patient Subgroup Post Hoc Analysis. *J Mult Scler.* 2014; 1:123.
15. Nelson F, Poonawalla AH, Datta S, Banuelos RC, Rahbar MH, et al. Association of Multiple Sclerosis Related Cognitive Impairment with an MRI-Derived Composite Score. *J Mult Scler.* 2014; 1:124.
16. Serag H, Abdelgawad D, Emara T, Moustafa R, El-Nahas N, et al. Effects of Para-Spinal Repetitive Magnetic Stimulation on Multiple Sclerosis Related Spasticity. *Int J Phys Med Rehabil.* 2014; 2:242.
17. Joanna S, Playford DE, Radford KA. What Is 'Early Intervention' for Work Related Difficulties for People with Multiple Sclerosis? A Case Study Report. *J Neurol Neurophysiol.* 2014; 5:252.
18. Thiruppathy K, Preziosi G, Bajwa A, Sharma P, Cerdeira M, et al. Multiple Sclerosis Related Bowel Dysfunction: Pathophysiology, Clinical Manifestation and Management. *J Neurol Neurophysiol.* 2014; 5:255.
19. Abdul Mannan Baig. Cloned Microglia with Novel Delivery System in Multiple Sclerosis. *J Stem Cell Res Ther.* 2014; 4:252
20. Elzbieta Miller and Marta Niwald. Novel Physiotherapy Approach for Multiple Sclerosis. *J Nov Physiother.* 2014; 4: 228
21. Vachová M, Novotná A, Mares J, Taláb R, Fiedler J et al. A Multicentre, Double-Blind, Randomised, Parallel-Group, Placebo- Controlled Study of Effect of Long-Term Sativex® Treatment on Cognition and Mood of Patients with Spasticity Due to Multiple Sclerosis. *J Mult Scler.* 2014; 1:122.
22. Berard JA, Walker LAS, Smith AM, Freedman MS. Longitudinal Comparison of Desktop and fMRI Scanner Versions of the Computerized Test of Information Processing in Multiple Sclerosis: A Pilot Study. *J Mult Scler.* 2014; 2:121.
23. Genova HM, Dobryakova E, Gonen O, Hillary F, Wylie G, et al. Examination of Functional Reorganization in Multiple Sclerosis using fMRI-Guided Magnetic Resonance Spectroscopy: A Pilot Study. *J Mult Scler.* 2014; 2:120.
24. Delgado SR, Lavi ES, Campos YA, Ortega M, Rammohan K, et al. Natalizumab Associated PML in a Multiple Sclerosis Patient: Excellent Response to Minimal Intervention. *J Mult Scler.* 2014; 1:119.
25. Reginald C. Adiele and Chiedukam A Adiele. Progressive Multifocal Leukoencephalopathy. *J Mult Scler.* 2014; 1:118
26. Sedighi B, Shafa MA, Abna Z, Ghaseminejad AK, Farahat R et al. Association of Cognitive deficits with Optical Coherence Tomography changes in Multiple Sclerosis Patients. *J Mult Scler.* 2014; 1:117.
27. Anbarasan D, Howard J, Ryerson LZ. Use of Maraviroc in the prevention and Treatment of Immune Reconstitution Inflammatory Syndrome in Natalizumab-Associated Progressive Multifocal Leukoencephalopathy. *J Mult Scler.* 2014; 1:116.
28. Iverson WO, Pavlovic D, Peterson I, Liu M. A Collaborative Approach to Addressing PML: The PML Consortium. *J Mult Scler.* 2014; 1:115.
29. Schutte C-M. Progressive Multifocal Leukoencephalopathy in Africa—A Review. *J Mult Scler.* 2014; 1:114.
30. David J. Libon, Dana L. Penney, Randal Davis, David S. Tabby, Joel Eppig, et. al. Deficits in Processing Speed and Decision Making in Relapsing-Remitting Multiple Sclerosis: The Digit Clock Drawing Test(dCDT). *J Mult Scler.* 2014; 1:113
31. Anja Gossmann, Paul Eling, Andreas Kastrup, and Helmut Hildebrandt. No Effect of Cooling on Cognitive Fatigue, Vigilance and Autonomic Functioning in Multiple Sclerosis. *J Mult Scler.* 2014; 1:112
32. Farooq O, Hojnacki D, Balos L, Weinstock-Guttman B. Recurrent Pseudotumoral Demyelinating Disease in an Adolescent Patient. *J Mult Scler.* 2014; 1:111.
33. Amico AP, Nisi M, Covelli I, Polito AM, Damiani S, et al. Efficacy of Proprioceptive Training with Prokin System in Balance Disorders from Multiple Sclerosis. *J Mult Scler.* 2014; 1:110.
34. Krájčík O, Bloigu R, Remes AM. High Frequency of Fractures in an Early Stage of MS. *J Mult Scler.* 2014; 1:109.
35. Kresimir Dolic. Progressive Form of Multiple Sclerosis. *J Mult Scler* 2014; 1: i104

36. V. E. Kalodimou. Multiple Sclerosis in a 23 Year Old Woman: Flow Cytometry Analysis. *J Mult Scler.* 2014; 1:i101
37. Saeed S, Amir Ali S, Oger Joe. The Use of Mesenchymal Stem Cells in the Treatment of Multiple Sclerosis: An Overview of Open Labels and Ongoing Studies. *J Neurol Neurophysiol.* 2014; 5: 219.
38. Wonita Janzen, Sharon Warren, Frank Hector, Frances Fenrich and Kenneth G Warren. The Relationship between Geomagnetic Disturbances and Multiple Sclerosis at the Edge of the Auroral Zone. *Epidemiol.* 2014; 4: 165.
39. Bansi J, Riedel S. Exercise Intensities in MS - Comparison between the Physiological Threshold Values of a Cardiopulmonary Exercise Test and the Estimated Values by Training Formulas. *Int J Phys Med Rehabil.* 2014; 2:212.
40. Persinger MA, Koren SA, St Pierre LS. Applications of Weak, Complex Magnetic Fields that Attenuate EAE in Rats to a Human Subject with Moderately Severe Multiple Sclerosis. *J Neurol Neurophysiol.* 2014; 5:213.
41. Ehrli N, Bakchine S. Yet a Lot to Consider Regarding Cognition in Multiple Sclerosis. *J Mult Scler.* 2014; 1:e103.
42. Haegert DG. Obstacles to Progress in MS: A Personal Story. *J Mult Scler.* 2014; 1:e102.
43. Dolic K, Bilic I, Buca A, Radovic D, and Titlic M. Differentiation of Tumefactive Demyelinating Lesions from Metastatic Brain Disease with FDG PET-CT: A Case Report. *J Mult Scler.* 2014; 1: 108.
44. Kalodimou VE. Multiple Sclerosis & Research. *J Mult Scler.* 2014; 1:107.
45. Balashov KE. Multiple Sclerosis: New Hypotheses Are Needed. *J Mult Scler.* 2014; 1:106.
46. Amaya S, Serge B, Igor S, Diana O, and Nathalie E. Abnormal Long-Term Episodic Memory Profiles in Multiple Sclerosis. *J Mult Scler.* 2014; 1:105.
47. Anagnostouli MC, Manouseli A, Artemiadis AK, Katsavos S, Fillipopoulou C et al. HLA-DRB1* Allele Frequencies in Pediatric, Adolescent and Adult-Onset Multiple Sclerosis Patients, in a Hellenic Sample. Evidence for New and Established Associations. *J Mult Scler.* 2014; 1:104.
48. Tsamopoulos NG, Kalodimou VE, and Vlachos S. Chronic Cerebrospinal Venous Insufficiency in Multiple Sclerosis: The Hydrostatic-Immune Paradigm and the Flow Cytometry as a Diagnostic Tool. *J Mult Scler.* 2014; 1:103.
49. Khatri BO, Tarima S, McQuillen MP, Kramer J, Dukic M et al. Plasma Exchange in Secondary Progressive Multiple Sclerosis: Twenty-Five Year Follow-Up Study. *J Mult Scler.* 2014; 1:102.
50. KrÅŕkki O, Bloigu R, Remes AM. High Frequency of Fractures in an Early Stage of MS. *J Mult Scler.* 2014; 1:109.
51. Schutte C-M. Progressive Multifocal Leukoencephalopathy in Africa – A Review. *J Mult Scler.* 2014; 1:114.
52. Yildiz M, Tettenborn B. Alemtuzumab: The Right Choice in the Management of Relapsing-remitting Multiple Sclerosis? *J Neurol Neurophysiol.* 2014; 5:196.
53. Sinha S, Karandikar NJ. Multiparameter Flow Cytometric Assays to Quantify Effector and Regulatory T-Cell Function in Multiple Sclerosis. *J Mult Scler.* 2014; 2:130.
54. Joanna S, Playford DE, Radford KA. What Is 'Early Intervention' for Work Related Difficulties for People with Multiple Sclerosis? A Case Study Report. *J Neurol Neurophysiol.* 2014; 5:252.
55. Kumar I, Verma A, Srivastava A, Shukla RC. Idiopathic Hypertrophic Pachymeningitis – MRI Diagnosis and Follow up. *J Neurol Disord.* 2015; 3:198.
56. Lahesmaa-Korpinen AM, Jalkanen SE, Chen P, Valo E, NÅŕez- Fontarnau J, et al. FlowAnd: Comprehensive Computational Framework for Flow Cytometry Data Analysis. *J Proteomics Bioinform.* 2011; 4: 245-249.
57. Kalodimou VE. Multiple Sclerosis & Research. *J Mult Scler.* 2014; 1:107
58. Badawi AH, Kiptoo P, Siahaan TJ. Immune Tolerance Induction against Experimental Autoimmune Encephalomyelitis (EAE) Using A New PLPB7AP Conjugate that Simultaneously Targets B7/CD28 Costimulatory Signal and TCR/MHC-II Signal. *J Mult Scler.* 2014; 1:131.
59. Bifulco M, Malfitano AM. Advances in Flow Cytometry Investigation of Cannabinoid CB2 Receptor Agonists in Multiple Sclerosis: Commentary. *J Mult Scler.* 2014; 1:128.

60. Tsamopoulos NG, Kalodimou VE, and Vlachos S. Chronic Cerebrospinal Venous Insufficiency in Multiple Sclerosis: The Hydrostatic-Immune Paradigm and the Flow Cytometry as a Diagnostic Tool. *J Mult Scler.* 2014; 1:103.
61. Tsamopoulos NG, Kalodimou VE, and Vlachos S. Chronic Cerebrospinal Venous Insufficiency in Multiple Sclerosis: The Hydrostatic-Immune Paradigm and the Flow Cytometry as a Diagnostic Tool. *J Mult Scler.* 2014; 1:103.
62. Hogan EL, Podbielska M, O'Keefe J. Implications of Lymphocyte Anergy to Glycolipids in Multiple Sclerosis (MS): iNKT Cells May Mediate the MS Infectious Trigger. *J Clin Cell Immunol.* 2013; 4:144.
63. Balashov KE. Multiple Sclerosis: New Hypotheses Are Needed. *J Mult Scler.* 2014. 1:106.
64. Wheeler CJ, Seksenyan A, Koronyo Y, Rentsendorj A, Sarayba D, et al. T-Lymphocyte Deficiency Exacerbates Behavioral Deficits in the 6-OHDA Unilateral Lesion Rat Model for Parkinson's Disease. *J Neurol Neurophysiol.* 2014; 5:209.
65. Tenenbaum SN and Garrahan JP. Review on Recent Advances in Multiple Sclerosis and Related Disorders. *J Neurol Neurophysiol.* 2014; S12:016.
66. Totaro R, Carmine CD, Carolei A. Tumefactive Demyelinating Lesions in Patients with Relapsing Remitting Multiple Sclerosis Treated with Fingolimod. *J Neurol Neurophysiol.* 2014; S12:006.
67. Scott TF. The Clinical Course of Multiple Sclerosis Needs to be Redefined in the Treatment Era of MS. *J Neurol Neurophysiol.* 2014; S12:003.
68. Pahan K. Multiple Sclerosis and Experimental Allergic Encephalomyelitis. *J Clin Cell Immunol.* 2013; 4:e113.
69. Kalodimou VE, Charalampopoulos G, Bekos V, Takis K, Ghiatas A, et al. Multiple Sclerosis in a 23 Years Old Woman Treated by Venous Angioplasty for Chronic Cerebrospinal Venous Insufficiency: A DNA Study by Flow Cytometry. *Cardiol Pharmacol.* 2013.
70. McLaughlin PJ, Zagon IS. A New Biotherapeutic Approach for the Treatment of Multiple Sclerosis. *Transl Med.* 2013; 3:e119.
71. Marian Simka. What Could Be a Primary Cause of Multiple Sclerosis: Is It an Autoimmunity Triggered by Chronic Protozoan Infection? .2013.
72. Freedman MS, Kaplan JM, Markovic-Plese S. Insights into the Mechanisms of the Therapeutic Efficacy of Alemtuzumab in Multiple Sclerosis. 2013.
73. Levin MC, Lee S, Gardner LA, Shin Y, Douglas JN, et al. Autoantibodies to Non-myelin Antigens as Contributors to the Pathogenesis of Multiple Sclerosis. *J Clin Cell Immunol.* 2013; 4:148.
74. Yonggang Sha. New Insights into S-nitrosylation in Multiple Sclerosis. *J Clin Cell Immunol.* 2013; 4: 147
75. Aruin AS, Mehendale K. Exercise Approaches to Ameliorate Fatigue in People with Multiple Sclerosis. *J Nov Physiother.* 2013; 3: 179.