

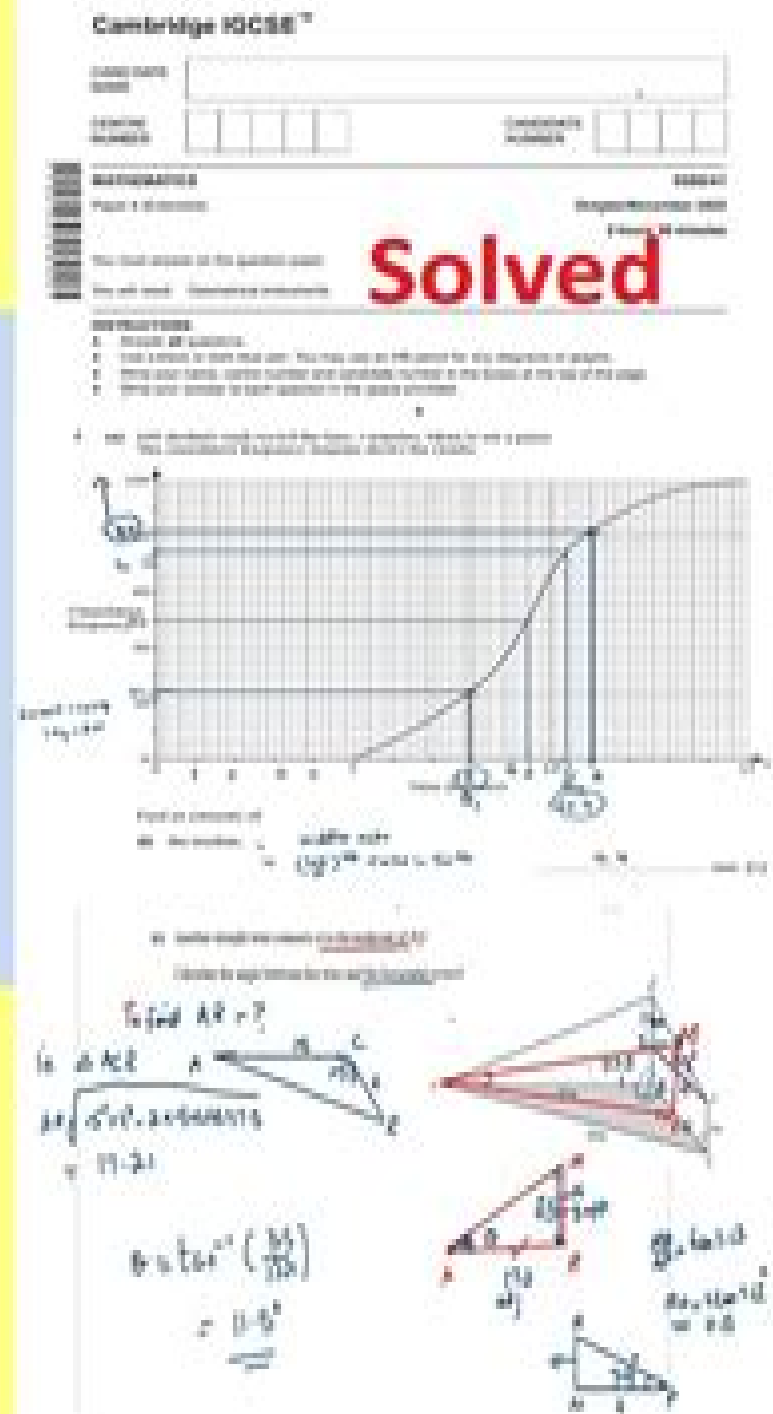
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EPA-450/2 ,1976-05 **Lymphocytes in MS and EAE: More than just a CD4+ World** Manu Rangachari,Nathalie Arbour,Steven M Kerfoot,Jorge I Alvarez,2017-10-10 Multiple sclerosis is degenerative disease of the central nervous system CNS in which myelin destruction and axon loss leads to the accumulation of physical cognitive and mental deficits MS affects more than a million people worldwide and managing this chronic disease presents a significant health challenge Multiple lines of evidence indicate that MS is an autoimmune disorder in which immune cells launch an inflammatory attack targeting myelin antigens Indeed myelin reactive T cells and antibodies have been identified in MS patients and in animal models namely experimental autoimmune encephalomyelitis or EAE that recapitulate many features of human disease Animal model studies have demonstrated that T cells are both necessary and sufficient to initiate and sustain CNS autoimmunity However most MS animal models rely on the role played by CD4 T cells and partially replicate the multiple aspects of MS pathogenesis Thus research in the past has focused heavily on the contribution of CD4 T cells to the disease process searching PubMed for MS AND CD4 yields twice the results as corresponding searches for CD8 or B cell and four times that for NK cells While CD4 T cells may represent the minimum requirement to mediate CNS autoimmunity it is clear that the immune response underlying human MS is far more complex and involves numerous other immune cells and subsets This is well illustrated by the observation that MS patients treated with an anti CD4 depleting antibody did not gain any clinical benefits whereas removal of several lymphocyte subsets using an anti CD52 depleting antibody has been shown to impede disease progression In particular the pathogenic role s of non CD4 T cell lymphocytes is relatively poorly understood and under researched despite evidence that these subsets contribute to disease pathology or regulation For example the observed oligoclonal expansion of CD8 T cells within the CNS compartment supports a local activation CD8 T cells with polarized cytolytic granules are seen in close proximity to oligodendrocytes and demyelinated axons in MS tissues The presence of B cells in inflammatory lesions and antibodies in the CSF have long been recognized as features of MS and Rituximab a B cell depleting therapy has been shown to be highly effective to treat MS Intriguingly the putative MS therapeutic reagent Daclizumab may function in part through the expansion of a subset of immunoregulatory NK cells NKT and T cells may also play a role in CNS autoimmunity given that they respond to lipid antigens and that myelin is lipid rich While different animal models recapitulate some of these aspects of human disease identifying appropriate models and measures to investigate the role of these less well understood lymphocytes in MS remains a challenge for the field This Frontiers research topic aims to create a platform for both animal and human focused researchers to share their original data hypotheses future perspectives and commentaries regarding the role of these less well understood lymphocyte subsets CD8 T cells B cells NK cells NK T cells T cells in the pathogenesis of CNS autoimmunity **Directory of Air Quality Monitoring Sites** ,1973 **Scientific and Technical Aerospace Reports** ,1969 Army Register United States. Adjutant-General's Office,1950 American

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