Effects of C-reactive protein and pentosan polysulphate on human complement activation.

Klegeris A, Singh EA, McGeer PL.

Kinsmen Laboratory of Neurological Research, University of British Columbia, Vancouver, Canada.

Complement (C) activation is believed to play an adverse role in several chronic degenerative disease processes, including atherosclerosis, myocardial infarction and Alzheimer's disease. We developed several in vitro quantitative assays to evaluate processes which activate C in human serum, and to assess candidates which might block that activation. Binding of C-reactive protein (CRP) to immobilized cell surfaces was used as a tissue-based method of activation, while immunoglobulin G in solution was used as a surrogate antibody method. Activation was assessed by deposition of C fragments on fixed cell surfaces, or by capture of C5b-9 from solution. We observed that several cell lines, including SH-SY5Y, U-937, THP-1 and ECV304, bound CRP and activated C following attachment of cells to a plastic surface by means of air drying. Treatment of human neuroblastoma SH-SY5Y cells with the reactive oxygen intermediates generated by xanthine (Xa) - xanthine oxidase (XaOx) prior to air drying or by hydrogen peroxide solutions after air drying, enhanced C activation, possibly through oxidation of the cell lipid membrane. Several C inhibitors were tested for their effectiveness in blocking these systems. Pentosan polysulphate (PPS), an orally active agent, blocked C activation in the same concentration range of 1-1000 microg/ml as heparin, dextran sulphate, compstatin and fucoidan. PPS may have practical application as a C inhibitor.

PMID: 12100726 [PubMed - indexed for MEDLINE]