EDITORIAL

Current Problems in Uveitis

The discovery in 1977 that a retinal protein (S antigen) could produce uveitis was a quantum leap forward. It rapidly led to the development of animal experimental models that have similarities to clinical entities such as sympathetic ophthalmitis, the VKH Syndrome or birdshot chorioretinopathy and by modulation of experimental techniques to other types of retinal vasculitis. A great deal is now known about retinal S antigen. Its part in the photochemical process has been identified, the molecule has been fully sequenced, comparison with other species shows it is a highly conserved molecule with only small inter-species differences and more recent research has identified the polypeptide sequences in the molecule which are particularly uveitogenic. The disease in animals is largely T cell mediated and there is now considerable experience with these polypeptide fragments in animal models. Other retinal proteins such as rhodopsin and opsin have been shown to be uveitogenic and, in this respect, interphotoreceptor retinoid binding protein (IRBP) is of particular interest and importance. This molecule, involved in the uptake of vitamin A, has been sequenced and the gene isolated and identified on chromosome 10. Uveitogenic sequences have been identified, one of which has been found to be the most potent uveitogenic substance so far known.

The similarity of the experimental disease, the potent uveitogenic properties of S antigen and IRBP and the similarities of their structure in different species would imply that these molecules are likely to be important in human disease. A number of studies have found antibodies to S antigen in various types of human uveitis but disappointingly these do not appear to correlate with disease type or activity. Furthermore sensitisation to S antigen can be found in normal healthy people although the sensitised lymphocytes are relatively few in number in the peripheral blood and of low affinity. The role of S antigen, if any, therefore in human disease is far from clear and at present the future lies in further clinical studies using more specific antibodies to the various uveitogenic subunits of S antigen and IRBP.

The clinician requires two things from the ocular immunologist—serological tests to differentiate one type of uveitis from another and some help in assessing disease activity and prognosis, the patient also wants the question 'why me?' answered. Retinal immunology is highly complex and full of interactions and cross reactions so the hope of picking out one aetiological antigen may be naive—rather like trying to understand the musical theme of a symphony orchestra by listening only, for instance, to the woodwind section. If one looks at other specialties tests such as rheumatoid factor or antinuclear antibodies are helpful in making a differential diagnosis (rheumatoid arthritis or SLE) and giving a rational basis on which to base some aspects of prognosis and treatment but they do not necessarily correlate with disease activity, and instances in clinical medicine such as Goodpasture's syndrome, where a single pathogenic antibody can be identified and correlated with the clinical response are still comparatively rare. Ocular toxoplasmosis has been a well recognised condition for over 30 years, the pathology is well known and disease activity easily assessed but although the dye test is helpful in substantiating a diagnosis neither it nor any other recognised serological test has been shown to reflect disease activity or relapse.

Once an aetiological agent is identified the even more fascinating problem of environmental triggering factors, genetics and 'why me?' remain to be solved. There are intriguing insights to this problem becoming available. Klebsiella bowel organisms have long been circumstantially suspected of playing a role in triggering attacks of acute anterior uveitis. It has recently been shown that there are complementary amino acid sequences in the HLA B27 and Klebsiella molecules (ARVO 1988) suggesting that molecular mimicry may have a role and, providing molecular evidence of a link to a triggering factor, but rather disappointingly in this particular study to seronegative arthritis, rather than acute anterior uveitis. Good clinical research in uveitis depends on the study of well defined diagnostic entities and the accurate assessment of disease activity. In this respect quantification of the ocular inflammatory response would have great benefits. This can be performed with fluorophotometry but is likely to be greatly simplified in future by non-invasive techniques such as the new Kowa Laser Cell and Flare Meter.

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