

Newsdesk

Susceptibility to autoimmune disease explained?

It is well known that susceptibility to autoimmune diseases such as multiple sclerosis and uveitis varies depending on the genetic background of the individual, but the mechanism whereby this occurs is unknown. Although conventional teaching has it that potentially autoreactive lymphocytes are deleted in the thymus during development, more recent findings have indicated that there are small numbers of autoreactive T cells present in the periphery and which have presumably escaped deletion in the thymus. The extent of thymic deletion of autoreactive T lymphocytes is dependent in some part on the expression of self antigens in the thymus and it has been shown that self antigens, such as retinal and CNS proteins, previously considered to be organ specific, are expressed at low levels in the thymus. Their expression in the thymus is thought to be important for the induction of tolerance and thus protection from autoimmune disease. A recent paper (*Nature Medicine* 2000;6:56–61) has reported a further twist to this tale. Proteolipid protein (PLP) is a major protein of myelinated nerve fibres and immunisation of animals with this protein combined with adjuvant produces a demyelinating disease with similarities to multiple sclerosis. PLP is composed of a number of antigenic peptides (epitopes) and some of these are expressed in the thymus on thymic epithelial cells. Intrathymic expression of PLP was largely restricted to the shorter splice variant of PLP, known as DM20. Expression of DM20 by thymic epithelium was sufficient to confer T cell tolerance not only to DM20 but to all other epitopes of PLP in a strain of disease resistant mice. In contrast, this major T cell activating epitope was expressed only in the central nervous system specific PLP, but not in the thymus, of disease susceptible mice. The authors suggest that the absence of this antigen from the thymus prevented susceptible mice developing tolerance to the disease and offers an explanation for the exquisite susceptibility of the latter strain of mice to experimental autoimmune encephalomyelitis. They further suggest that as PLP expression in the human thymus is also restricted to the DM20 isoform, these findings have risk implications for multiple sclerosis.

NSAIDs may be toxic to cornea

Recent reports suggest that some non-steroidal anti-inflammatory drugs may be toxic to the cornea especially if used frequently or intensively. As reported in *Eyenet*, the magazine of the American Academy of Ophthalmology, a survey conducted by the American Society of Cataract and Refractive Surgery has found at least 200 cases of corneal toxicity related to the use of NSAIDs. No relation with associated corticosteroid use was noted but patients with dry eye were more at risk. Both diclofenac and Acular (ketorolac) were implicated. According to *Eyenet*, Alcon, the suppliers of generic diclofenac, have suspended distribution of the drug while investigating these reports.

Harold Ridley honoured

Harold Ridley, FRS, known worldwide for the introduction of intraocular lens implants, arguably the most significant development in

ophthalmic surgery of the last century, has been honoured with a knighthood in the latest round of UK national honours. Donald Munro, managing director of Rayner the firm that manufactured the first intraocular lenses, said "At last, Harold Ridley has received the recognition he deserves—this is truly a life changing operation that has benefited the world. This is a great British achievement, the foundation of an industry...". Ridley's observation that fighter pilots during the second world war, who suffered intraocular injuries involving the deposition of plastic shards in the eye from their shattered cockpit canopies and failed to develop significant intraocular inflammation, led him to believe that the intraocular compartments could tolerate such materials. So it has proved.

An accommodating IOL

Following Harold Ridley's pioneering development of the intraocular lens (IOL) for cataract, the next challenge has been to develop an accommodating intraocular lens that would cope with the problem of presbyopia. In the recent edition of *Eyenet*, a report by Laslo Dosa indicated that an accommodating intraocular lens is in phase I clinical trials. Made of a "new, unique blend of silicone" it is placed vaulted posteriorly against the vitreous face and hinges forward just outside of the optic on the haptic to allow maximum forward movement for near vision. The lens moves forward about 1 mm accounting for about 2 dioptres of accommodation, according to Stephen Slade who is conducting the trial. The current study involves 16 eyes in 15 patients who had mature cataracts.

Minimising leakage from blood vessels

Several retinal diseases are characterised by leakage from retinal and/or choroidal vessels. The resulting macular oedema is a major cause of visual loss in diseases such as diabetic retinopathy, posterior uveitis, and age related macular disorders. In some of these diseases growth factors such as vascular endothelial growth factor (VEGF) are strongly implicated not only in the growth of new vessels but also in the initial leakage from these vessels. Indeed, VEGF was first identified as an inducer of vascular leakage in tumours and inflammatory conditions before it was recognised as an angiogenic factor. More recent studies have identified other growth factors such as angiopoietin 1 and 2 and Tie 1 and 2 in regulating new vessel growth, and several research programmes are directed at determining the role of these novel factors in conditions such as retinopathy of prematurity and diabetic retinopathy. A recent study has shown in transgenic mice overexpressing angiopoietin or VEGF that, while both growth factors can induce new vessel growth, angiopoietin prevents vascular leakage, in contrast with VEGF which has the opposite effect (*Science* 1999;286:2511–14). In addition, inflammatory agents were unable to induce leakage in vessels in Ang1 overexpressing mice. In strains of mice which were bred to coexpress Ang1 and VEGF there was an additive effect on angiogenesis but leakage resistant vessels typical of Ang1 alone persisted. The authors suggest that selective use of Ang1, therefore,

may be useful for reducing microvascular leakage in diseases in which the leakage results from chronic inflammation (such as uveitis), in contrast with diabetic retinopathy in which inhibition of VEGF might be preferable.

3% of homeless have TB

The UK charity Crisis indicated that there appeared to be a rise in the incidence of TB in homeless individuals attending their Crisis Open Christmas shelter during December 1999. Apart from the fact that there was an increase in the number of visits by 20% to 878 compared with the same period in 1998, the rise in TB incidence from 1/50 of this group to 1/33 reflected a worrying trend. Crisis is the UK national charity for single homeless people—that is, those with no legal rights to housing. It researches, develops, and partners schemes to provide help where it is most needed at whatever stage of homelessness—from emergency help on the streets, through hostel accommodation, permanent housing, and resettlement support.

Uveitis patient information group

Uveitis, particularly posterior uveitis (better termed posterior segment intraocular inflammation), is a surprisingly common cause of visual loss in all age groups and estimates of incidence suggest that it is as frequent a cause of visual handicap as diabetic retinopathy. Despite this, very little information concerning uveitis is available generally and especially to the public at large or even to patients with sight threatening posterior segment intraocular inflammation. This is partly due to the wide spectrum of clinical entities which can be categorised as posterior segment intraocular inflammation and the tendency for causes of blindness to be recorded by the specific clinical entity rather than the generic "uveitis" or "intraocular inflammation" title. However, many of these conditions can respond to appropriate and adequate therapy and, in many cases, despite the clinical heterogeneity, the treatment approach follows similar principles. Patients with uveitis would benefit from information on this complex set of conditions and a new patient information group, the Uveitis Information Group, has been established with a website address for interested individuals including healthcare professionals and patients (www.uveitis.net).

Eprints

Publishing scientific literature will dramatically change in the near future. This is mainly because of the effects of the internet. Recent developments include the "eprint", which is a posting of a completed study on a website before submission for peer review. Eprints are already the norm in other scientific fields such as high energy physics and astronomy, and are coming fast to medicine. The *BMJ* has already launched its eprint server on the internet and many specialist journals are likely to follow suit, including the *BJO*. In a sense this sort of publishing will be a return to the early days of printed journals when formal peer review was rare if it occurred at all and peer review meant comment by letters to the editor from the readership. Eprints will be accompanied by the full peer reviewed article appearing later in the journal if accepted.