Sir,

**Current concepts and future directions in the pathogenesis and management of non infectious uveitis**

We read with interest the excellent overview by Lee *et al*[1] on 'Current concepts and future directions in the pathogenesis and treatment of non-infectious intraocular inflammation'. The authors have remarked about the 'swing of intraocular inflammation from infective to inflammatory over last century'. However, with current novel diagnostic tools more non infectious intraocular inflammatory diseases have been recognized and treated as infective uveitis.[2] According to Russell Read, infectious uveitis accounted for 13 to 21 percent of the total uveitis cases seen at tertiary referral centers.[3] Infectious uveitis can become latent, smoldering, and mimic autoimmune uveitis. Although autoimmune uveitis responds to corticosteroids or immunosuppressives, such treatment worsens infectious uveitis.[2] The authors have also highlighted the fact there is enough compelling data to suggest trigger of innate immunity by hidden concomitant infection.[1] From that perspective, infectious causes should always be considered in all patients with uveitis. The differential diagnosis includes herpes, syphilis, toxoplasmosis, tuberculosis, bartonellosis, Lyme disease, and others.[2] Air travel, immigration, and globalization of business have overturned traditional pattern of geographic distribution of infectious diseases, and therefore one should work locally but think globally.[2] Lee *et al*[1] have remarked on dysregulation of immunity within the eye as a guiding principle for current management strategy.[1] On the contrary, with more infective entity being recognized, the focus should be more on recognizing and targetting the infective stimulus. Unfortunately, most infectious causes are only possible to detect by using very specific detection methods. Furthermore, it is often necessary to study a sample from with-in the eye to get a proper diagnosis.[2] As mentioned by the authors in the current series, anterior chamber tap can be performed to carry out PCR for infective agents but still in developing countries it is not readily available and most of the diagnosis is clinical. When non-infectious uveitis is in the differential, empiric corticosteroids must sometimes be used, at great risk, if clinical examination, ancillary testing, and any available intraocular diagnostic tests have failed to confirm a diagnosis.[4] Failing to give infectious etiologies a place on the diagnostic 'radar screen' and failure to consider infective etiology before starting immunosuppressive or biologic agents can have serious consequences to the patient.

**Conflict of interest**

The author declares no conflict of interest.

**References**

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Sir,

**Response to Dr Agrawal**

We thank Dr Agrawal[1] for his correspondence, which helpfully highlights the important role of infectious pathogens in the aetiology, diagnosis, and treatment of uveitis. Although the title of our review explicitly limits its scope to non-infectious intraocular inflammation, we endorse his emphasis on the importance of excluding treatable infectious uveitides before embarking on treatment with immunosuppressive agents. However, while acknowledging wide global variation in the burden of infectious diseases, historical surveys endorse our assertion that in Western populations the balance has firmly swung in favour of autoimmunity and autoinflammation—in Guyton and Woods[2] (USA), 1941 series, over 60% of uveitis cases were due to tuberculosis or syphilis, whereas half a century later, Rothova *et al*[3] (Netherlands) reported that these infections accounted for less than 3% of their cohort.

It is also important to reiterate the potential crossover between infectious and autoimmune/autoinflammatory diseases, as outlined in our overview of immunopathology; in particular the role of molecular mimicry and the key contribution concomitant infection has in giving innate immune permission to the antigen-specific adaptive immune responses we observe in the eye. We also increasingly have access to molecular biological technologies, which enable us to exclude direct intraocular infection from aqueous or vitreous biopsies, and in the absence of a proven pathogen we strongly advocate appropriate immunosuppression to maintain vision.

**Conflict of interest**

The authors declare no conflict of interest.

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