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Why do we treat? Defining disease control in JIA associated uveitis

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In a recent issue of *The Journal of Rheumatology*, Berard et al¹ reported on the development of the Canadian recommendations for the screening, monitoring, and treatment of uveitis associated with juvenile idiopathic arthritis (JIA).¹ The guidance from this national multidisciplinary JIA-associated uveitis working group had a welcome and necessary focus on the importance of disease control but omitted a definition of controlled disease.

Tight disease control is a central paradigm for the management of JIA.² The aim of treatment, for any disease, is prevention or minimisation of the mortality or morbidity conferred by the disorder. For children with chronic anterior uveitis, the predominant form of ocular inflammation seen in JIA, a key conferred morbidity is sight loss.³ The strongest predictor poor visual outcome is poor vision at disease detection³ but the strongest modifiable predictor post diagnosis is ongoing uncontrolled disease.³ Robust definitions of disease control support clinical practice by providing a target against which to judge response to therapeutic intervention. Standardisation of these definitions supports the collation of clinical records across multicentre sites in rare disease research, providing the sample sizes necessary to model the association of child or treatment level factors on outcomes of interest.

In 2005, the Standardised Uveitis Nomenclature (SUN) International working group reached a consensus on how to grade anterior chamber ocular inflammation: using the number of inflammatory cells visible by a clinician through a central 1mm beam on slit lamp biomicroscope examination (table 1).⁴ A score of 0 SUN does not equate to an anterior chamber wholly free of inflammatory cells, but instead an eye with a degree of inflammation sufficiently low as to permit a cell free examination using a centrally focused beam. Levels of 1+ SUN anterior chamber cell counts are classified as active disease by the clinical community.⁴ However, the threshold for inactive disease, and thus the aimed for outcome

following medical intervention, differs amongst international groups. The American College of Rheumatology defines controlled JIA associated anterior uveitis as anterior chamber inflammation at the level of SUN grade <1+ anterior chamber cells (ie inclusive of grade +0.5) without new complications due to active inflammation.⁵ Conversely, the Single Hub and Access point for pediatric Rheumatology in Europe (SHARE) group (later updated as the Multinational Interdisciplinary Working Group for Uveitis in Childhood, MIWGUC) defined inactive disease as “0 (zero) inflammatory cells in the anterior chamber”.^{6,7} The Australian and New Zealand Juvenile Idiopathic Arthritis-Uveitis Working Group could not reach a consensus on the threshold for inactive disease.⁸

The absence of an international consensus on defining inactive disease may reflect the shortcomings of the current method of quantifying disease. Clinically inactive eyes (i.e., SUN 0, with no cells seen in a centrally focused slit lamp beam) can demonstrate the presence of inflammatory cells on wider examination of the anterior chamber (figure 1). At all levels of inflammation, slit lamp examination has been shown to be subjective, with wide inter and intra-observer variability.⁹ The work underway on the clinical validation of objective, sensitive imaging-based inflammation quantification may provide the evidence base necessary to reach some degree of consensus around inactive versus active disease in childhood anterior uveitis.¹⁰ Until then, investigators should aim to specify, when discussing disease control in anterior uveitis, their chosen definition of control, to aid those seeking to implement study recommendations within clinical practice, or to undertake clinical research for this rare and impactful disorder.

Figure 1. High resolution imaging of the anterior chamber with optical coherence tomography.

Inflammatory cells in a clinically inactive eye circled by dashed line. Anterior ocular anatomical landmarks are labelled.

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